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RABIES.

A REVIEW OF RECENT ARTICLES. XXVII.*

i. *Virus.*

It is a curious fact that, since Noguchi claimed in 1913 to have cultivated the virus of rabies, no conclusive confirmation should appear for 24 years, and that now two sets of workers, almost simultaneously should afford that confirmation working independently, but using almost identical methods of cultivation. These are KANAZAWA[1, 2] in Tokio, and WEBSTER and CLOW[3] at the Rockefeller Institute for Medical Research. In both cases the culture medium is a Tyrode solution containing fragments of embryonic rabbit brain. The respective prescriptions are :—

Japanese.

Tyrode 5 per cent.	100 cc.
Embryonic rabbit brain (25th day) emulsion	4 to 5 drops

American.

Tyrode 4 per cent. containing 10 per cent. normal monkey brain serum	50 cc.
Minced mouse embryo brain	0·02 cc.

After inoculation with virus, the supernatant fluid is withdrawn at intervals of 3 or 4 days and transferred to a second culture flask. KANAZAWA found that the virulence of the subculture, at first relatively high, falls rapidly, and then increases from the 3rd day, reaching a maximum higher than the original titre between the 4th and 6th days. So far KANAZAWA has passaged fixed virus through 26 passages or over a period of 119 days. He finds that the properties of the cultivated virus are unchanged, as regards neutralization by immune serum and as regards absence of negrigenesis. WEBSTER and CLOW have carried a skunk strain through 16 serial subcultures, and

*For the twenty-sixth of this series see 1937, Vol. 34, p. 230.

[1] KANAZAWA (K.). Sur la culture *in vitro* du virus de la rage. (Deuxième mémoire.)—*Japanese Jl. Experim. Med.* 1937. Feb. 20. Vol. 15. No. 1. pp. 17–27. With 2 figs.

[2] KANAZAWA (K.). Sur la culture *in vitro* du virus de la rage.—*Japanese Jl. Experim. Med.* 1936. Oct. 20. Vol. 14. No. 5. pp. 519–522.

[3] WEBSTER (Leslie T.) & CLOW (Anna D.). Propagation of Rabies Virus in Tissue culture and the Successful Use of Culture Virus as an Antirabic Vaccine. —*Science.* 1936. Nov. 27. Vol. 84. No. 2187. pp. 487–488.

also a dog strain. They state that " the culture virus protects mice against street virus, and that a single peritoneal inoculation is innocuous and within 10 days makes an animal resistant to 100 intracerebral fatal doses of street virus of homologous or heterologous strains. They are engaged in studying the possibility of using tissue culture virus as an antirabic vaccine.

In a preliminary note PERAGALLO[4] states that he has succeeded in cultivating the virus on the chorion-allantoid membrane of the chick. The procedure adopted followed the same lines as have been used for the cultivation of vaccinia. Serial passage has been carried out—Negri bodies are found in the epithelial cells of the membrane, and the membrane itself is capable of infecting test animals. Subcultures of both fixed and street virus have been made. The numbers of passages are not given.

The characteristics of the strain of fixed virus employed at Hanoi (Indo-China) have been investigated by GENEVRAY and DODERO.[5] The strain is in its 2,033rd passage, and is of high virulence (paralysis of rabbit on the 4th or 5th day). It differs from the original Paris strain in various respects. It is rather less aggressive when given subcutaneously ; its resistance to desiccation and to glycerine has diminished, but in a considerably less degree than has been the case in other institutes. In its resistance to ether it is comparable to the Tangier strain. In the last section of the paper it is shown that segments of cord embedded in paraffin (melting point 56–58°) retain virulence up to at least 60 days.

The strain of fixed virus in use at Lille continues to change. GRYSEZ[6] states that cords preserved at 23°C. are becoming less resistant to the action of glycerine. After 15–25 days at 23° in glycerine virulence is completely lost. It thus becomes necessary to alter the scheme of dosage in the treatment of bitten persons. Various modifications are suggested, in which either the temperature or the period of drying of the cords is reduced.

REMLINGER and BAILLY[7] recall the fact that HÖGYES started his dilution method with a virus whose lethal dose was 0·2 cc. of a 1/5000 dilution. The authors found in 1934 that the corresponding dilution for the Tangier strain was 1/900,000. They have now examined 11 viruses of Moroccan origin, and find that their virulence was very variable, the titre varying from 1/200 to 1/100,000. This variation is ascribed not to the effect of dilution but to the nature of the particular strain.

The detail of the experiments carried out with the 11 strains is given in a subsequent paper.[8]

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[4]PERAGALLO (Italo). Richerche sulla possibilità della cultura del virus rabico nella membrana corion-allantoidea dell'embrione di pollo. (Nota preventiva.) —*Giorn. di Batteriol. e Immunol.* 1937. Mar. Vol. 18. No. 3. pp. 289–290. English summary (1 line).

[5]GENEVRAY (J.) & DODERO (J.). Le virus rabique fixe de l'Institut Pasteur de Hanoi.—*Ann. Inst. Pasteur.* 1936. Dec. Vol. 57. No. 6. pp. 638–651. With 2 graphs.

[6]GRYSEZ (Victor). Action de certaines températures sur la conservation de l'activité du virus fixe de Pasteur.—*Ann. Inst. Pasteur.* 1937. Feb. Vol. 58. No. 2. pp. 125–129.

[7]REMLINGER (P.) & BAILLY (J.). Action de la dilution sur les virus rabiques de rue.—*C. R. Soc. Biol.* 1937. Vol. 124. No. 1. pp. 7–9.

[8]REMLINGER (P.) & BAILLY (J.). Action de la dilution sur les virus rabiques de rue.—*Ann. Inst. Pasteur.* 1937. Apr. Vol. 58. No. 4. pp. 377–387.

In 1910 (*Arch. de Méd. expér. et d'anat. pathol.*) REMLINGER pointed out that fixed virus enveloped (enrobé) in powdered bicarbonate of soda induced symptoms of furious rabies. REMLINGER and BAILLY[9] have repeated this observation and find that the Tangiers strain of fixed virus which invariably causes dumb rabies in the rabbit, induces fury when enveloped in bicarbonate. This has been observed in the rabbit and in the dog; in the cat, the guineapig and the rat there is less marked excitation. Even in animals which have shown the most marked excitability, Negri bodies are however absent in the horn of Ammon, and in the oculomotor nucleus. The authors discuss the nature of this phenomenon. They refer to the observation of MILLISCHER and MARTEAU (this *Bulletin*, 1937, Vol. 34, p. 237) that frozen cords have the same propensity, and conclude that it is more likely to be a physico-chemical phenomenon of which the nature is difficult to determine, than a return of the fixed virus to its original street form.

GERLACH and SCHWEINBURG[10] contribute a further section to their series of papers on Aujeszky's disease, published partly in the *Wien. Klin. Woch.* and partly (for veterinary consumption) in the *Ztschr. f. Infektionskr. d. Haustiere.* This group of papers forms a comprehensive study of the behaviour of numerous strains of the virus, and experimental results are recorded in detail. The ground covered is so wide that it is impossible to deal with it in a review. The main conclusions are those which have already been accepted.

A paper on the same subject by MANNINGER and MARCIS,[11] stresses the fact that pseudorabies reaches the central nervous system by way of the blood, and not along the nerve paths.

A case of pseudorabies (Aujeszky) in a dog is reported from Tunis by CORDIER and MÉNAGER.[12] A very thorough examination of the characteristics of the virus in question has been made, and in this the authors have received the advice and encouragement of REMLINGER. Its effects have been observed in the rabbit, the guineapig, and the pigeon, and numerous subpassages have been made. These leave the diagnosis of pseudorabies beyond doubt.

The urea content of the blood in 4 cases of pseudorabies in cattle has been examined by ROSSI.[13] A definite and rapid increase is found to occur. The chlorides are not appreciably modified—and the excretion of urea by the urine remains normal.

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[9]REMLINGER (P.) & BAILLY (J.). Modifications de la symptomatologie de la rage paralytique déterminées par l'enrobage du virus dans le bicarbonate de soude.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 34. pp. 953–955.

[10]GERLACH (Franz) & SCHWEINBURG (Fritz). Experimentelle Untersuchungen ueber die Aujeszkysche Krankheit (Pseudowut). II. Mitteilung.—*Ztschr. f. Infektionskr. d. Haustiere.* 1936. Dec. 8. Vol. 50. No. 2–3. pp. 86–128.

[11]MANNINGER (R.) & MARCIS (A.). Versuche mit dem Erreger der Aujeszkyschen Krankheit.—*Ztschr. f. Infektionskr. d. Haustiere.* 1937. Apr. 12. Vol. 51. No. 1. pp. 25–32.

[12]CORDIER (G.) & MÉNAGER (J.). Premier cas "africain" de maladie d'Aujeszky.—*Bull. Acad. Méd.* 1937. May 11. 101st Year. 3rd Ser. Vol. 117. No. 18. pp. 532–535.

[13]ROSSI (Paul). L'urée sanguine chez les bovins atteints de maladie d'Aujeszky.—*C. R. Soc. Biol.* 1937. Vol. 124. No. 8. pp. 706–707.

ii. *Symptoms and Diagnosis.*

A case of human rabies is reported from Nigeria by CRAWFORD[14].

An interesting and unexpected point comes to light in a paper by HORGAN and MCKINNON.[15]

It will be remembered that the rôle of the oculomotor nucleus as a seat of election for Negri bodies was pointed out by THOMAS and JACKSON (this *Bulletin*, 1931, Vol. 28, p. 744). This result was confirmed by NICOLAU and KOPCIOWSKA (1932, Vol. 29, p. 600 and 1933, Vol. 30, p. 575), and by MURATOWA (1935, Vol. 32, p. 173) who showed that the first appearance of Negri bodies is not in the horn of Ammon, but in the mid-brain. It may be remembered that the reviewer invited "those who have access to the necessary material to put these statements to the test, and to publish their findings, as the matter is of considerable importance" (1931, Vol. 28, p. 745). HORGAN and MCKINNON have collected the results of the examination of the brains of 37 animals suspected to have died of rabies. These may be classified as follows :—

Negri bodies present in—

Hippocampus and midbrain	10
Hippocampus only	8
Midbrain only	0
In neither situation	19
	37

Of the 37, 3 were donkey's brains, 1 a sheep's brain, another that of a rabbit inoculated from a human case, and the remainder were from dogs. The authors point out that the results obtained by the former workers were all from the brains of rabbits and mice which had been experimentally inoculated, whereas their own results were obtained from the brains of naturally infected animals, the majority of which were dogs. They claim that for the diagnosis of rabies in the naturally infected dog, the hippocampus is superior to the midbrain. Further work should clearly be done to find out the exact cause of the apparent discrepancy.

iii. *Pathology.*

The presence of intravascular bodies in the brain and cord of animals (rabbits, guineapigs, monkeys and dogs) is described by COLES.[16] The bodies are found in the endothelial cells of the small blood vessels of the brain. The method of staining employed was that of Giemsa. The bodies are "round or oval, rarely irregular in shape, and generally stained blue. They varied in size . . . being about ½–1 μ in diameter, but larger forms are also met with, some reaching 5 or even 6 μ . . . . The great majority show no structure, but in some a spot was seen situated in the centre or at one side, and this was deeper and

[14]CRAWFORD (R. P.). Notes on a Case of Human Rabies.—*West African Med. Jl.* 1936. Oct. Vol. 9. No. 1. p. 20.

[15]HORGAN (E. S.) & MCKINNON (R. M.). A Comparison of the Mesencephalon and Hippocampus as Sites of Election for Negri Bodies in Rabies.—*Jl. Hygiene.* 1937. Apr. Vol. 37. No. 2. pp. 340–344.

[16]COLES (Alfred C.). Intra-Endothelial Bodies in the Vessels of the Brain and Spinal Cord in Rabies.—*Jl. Path. & Bact.* 1937. Mar. Vol. 44. No. 2. pp. 315–319. With 12 figs. on 1 plate.

darker in colour but still blue or reddish blue." Sometimes clusters of bodies were seen which might represent division forms. The bodies "were found only in the small and medium vessels of the brain... never in the smallest capillaries, and practically never outside a vessel. In many instances it was at once obvious that they were situated in the endothelial cells of the vessel." "The granules are certainly not artefacts, pigment granules or mast cell granules." "Their position . . . . suggests a similarity to the Rickettsia parasites found in typhus." From an examination of slides kindly furnished by the author, the reviewer subscribes to the above description.

In a group of three communications MANOUÉLIAN[17] discusses the enervation of the face in relation to rabies. It is well known that bites on the face are much more dangerous than bites in other regions. The author points out that in addition to the recognized sympathetic ganglia related to the trigeminal nerve, "endoneurocytes" are found in its sensory branches. These may be isolated or in groups, in some cases forming actual ganglia. "What is the nature of these cells, are they sympathetic or sensory or both together? That remains for future research." But the important point is that the endoneurocytes may contain Negri bodies, and that the cells themselves undergo the same cytological changes as are seen in Rabies. The extreme gravity of face bites is thus due to the relative excess of neurones in the face as compared with other localities.

In the second place MANOUÉLIAN[18] finds that the cranial nerves, particularly the fifth, possess a higher degree of virulence than the spinal nerves. This is another consequence of the presence of intra-nervous cells in the cranial nerves. Inoculation of a sensory nerve of the face is, in fact, inoculation of ganglionic tissue.

In a third communication MANOUÉLIAN[19] points out that just as the virulence of the saliva is due to the shedding of neurones into the secretion, so also may virulent neurones be released from the tongue by a fissure or abrasion.

iv. *Methods of Treatment and Statistics.*

SAVAGNONE[20] has investigated the immunizing properties of a new type of filtered virus. The filtrate is obtained as follows. To an emulsion prepared by Puntoni's method are added small quantities (1–2 per cent.) of powdered animal charcoal. The charcoal sinks to the bottom, the supernatant fluid is aspirated off, and is then after dilution with one-third of an isotonic solution passed through a Berkefield V bougie. This filtrate was found to have retained its infecting and its immunizing properties. The author has tested it on the guineapig, and on the dog and suggests that its use might be extended to man. He thinks that it is possible that the liability to post-vaccinial sequelae may in this way be reduced.

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[17] MANOUÉLIAN (Y.). Haute gravité des morsures de la face dans la rage. Endo-neurocytes du trijumeau.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 32. pp. 771–773. With 1 fig.

[18] MANOUÉLIAN (Y.). Virulence des nerfs de la face au cours de la rage.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 32. pp. 773–774.

[19] MANOUÉLIAN (Y.). Neurones sympathiques périphériques de la face; leur rôle au cours de la rage.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 35. pp. 1084–1086.

[20] SAVAGNONE (Lucio). Sul potere patogeno ed immunizzante di un nuovo filtrato rabbico.—*Giorn. di Batteriol. e Immunol.* 1937. Mar. Vol. 18. No. 3. pp. 368–380. English summary (7 lines).

It is reported by VAZ[21] that of 3,643 persons treated at 276 different centres by vaccine prepared according to Puntoni's method and supplied from the parent institute at San Paulo (Brazil), none developed rabies.

The statistics of antirabic treatment from the various institutes over the world, for the year 1934, collected by the League of Nations are reviewed by MCKENDRICK.[22] This is the seventh review of the series and relates to 110,884 treated persons, of whom 335 died of rabies in spite of treatment (0·30 per cent.). The statistics are tabulated according to the various characteristics laid down by the Paris Rabies Conference, and in addition to those relating to the year under review the combined figures collected during that and the preceding six years are treated as a whole. With regard to the comparative efficiencies of the different methods of treatment as immunizing agents, it appears from the evidence so far available, that there seems to be little to choose between the cord, dilution, killed phenol, heated and killed ether methods, and that if anything the system in which dilution methods are reinforced in severe cases by ALIVISATO's ether vaccines has yielded slightly better results than the other methods. A new method of dealing with statistics of this nature, and of arriving at an estimate of comparative efficiency has been employed. Some interesting points emerge as regards paralytic accidents. These have been subdivided into fatal and non-fatal. It appears that both fatal and non-fatal accidents are relatively infrequent amongst those treated by killed phenol, killed ether and heated vaccines, the incidence rate for fatal accidents being of the order of 0·003, and for non-fatal 0·008 per cent. ; that both fatal and non-fatal accidents are relatively frequent amongst those treated by FERMI's original vaccine, the rates being 0·05 and 0·016 per cent. respectively ; that with treatment by cords fatal accidents are relatively infrequent (0·003 per cent.), whilst non-fatal are relatively frequent (0·028 per cent.) ; and that with dilution treatment accidents are relatively frequent and usually fatal (0·03 per cent. for total and 0·01 per cent. for non-fatal), whilst with the mixed method (dilution + Alivisato's) they are relatively infrequent but usually non-fatal (0·004 for total and 0·046 for non-fatal). This last result is a curious one, and so far no explanation is forthcoming.

v. *Rabies in Animals.*

TORRES and LIMA[23] report further observations on rabies in the vampire bat (for previous papers see this *Bulletin*, 1937, Vol. 34, p. 230). From these experiments it appears that a bat which on account of a high natural resistance to infection has become a carrier, may eliminate the virus up to about 4 months, and so infect other animals which it bites, and even other bats with whom it has been in contact. The

[21] VAZ (Eduardo). Santa Casa e serviço anti-rabico.—*Ann. Paulist. Med. e Cirurg.* 1936. Nov. Vol. 32. No. 5. pp. 437–440.

[22] MCKENDRICK (A. G.). A Seventh Analytical Review of Reports from Pasteur Institutes on the Results of Anti-Rabies Treatment.—*Bull. Health Organisation.* (League of Nations.) Geneva. 1937. Feb. Vol. 6. No. 1. pp. 17–55.

[23] TORRES (Sylvio) & LIMA (E. de Queiroz). A raiva e os morcegos hematophagos. Morcegos que resistem á infecção tornam-se portadores e eliminadores de virus ?—*Rev. Depart. Nac. da Producção Animal.* Rio de Janeiro. 1936. Dec. Vol. 3. Nos. 1–6. pp. 165–174. English summary.

proportion of experimentally infected bats which proved resistant was 4 out of 9, whilst the proportion of successful infections from bat to bat was 2 out of 4.

Another series of observations on bat infection is given by TORRES[24]. Six hungry bats did not bite a pup which shared their cage during a period of 3 days—and, similarly, two hungry bats did not bite a dog suffering from paralytic rabies over a period of 2 days. On the other hand two out of three bats which had shared the cage of a goat in the first day of rabies sickness became infected.

The literature on rabies in the bat continues to increase rapidly.

PAWAN[25] adds to previous researches to which reference has already been made (this *Bulletin*, 1936, Vol. 33, p. 742). He now studies the course of the infection in experimentally inoculated bats.

The protocols of the various experiments are given in detail. The incubation period after artificial inoculation is variable. Various clinical types were observed: (1) typical furious rabies, ending in paralysis and death; (2) typical paralytic rabies, ending fatally; (3) a furious form followed by recovery; (4) a furious form ending fatally without an intermediate paralytic stage; (5) a form in which the bats die suddenly without previous evidence of illness; (6) a latent form of infection. Once paralytic symptoms appear there is no recovery. It is thus seen that "bats may become carriers of rabies after 'recovery' from the furious form of the disease. In this state they may remain capable of spreading infection by their bites for prolonged periods."

JAUFFRET[26] describes a campaign against rabies in the dog conducted in CAMBODIA (Indo-China). 385 dogs have been inoculated with a formolated vaccine. Of these 5 died, but only one of the deaths could be ascribed to the effects of vaccination. The author emphasizes the importance of destruction of stray dogs, and progressive vaccination of the remaining dog population.

JAKEMAN[27] discusses some general points in the control of rabies in animals.

The difficulty of obtaining quantitative results as regards the degree of immunity in animals is discussed by WEBSTER[28]. An intradural test dose is usually overwhelming, whereas the effect of peripheral dosage is difficult to measure. "These technical difficulties have now been overcome in part by finding that special strains of mice bred for susceptibility to virus infections are 10 to 100 times more susceptible

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[24]TORRES (Sylvio). A raiva e a infecção natural dos morcegos hematophagos.—*Rev. Depart. Nac. da Producção Animal.* Rio de Janeiro. 1936. Dec. Vol. 3. Nos. 1–6. pp. 183–186. English summary.

[25]PAWAN (J. L.). Rabies in the Vampire Bat of Trinidad, with Special Reference to the Clinical Course and the Latency of Infection.—*Ann Trop. Med. & Parasit.* 1936. Dec. 23. Vol. 30. No. 4. pp. 401–422. [20 refs.]

[26]JAUFFRET (R.). Une campagne de vaccination contre la rage du chien au Cambodge.—*Arch. Inst. Pasteur d'Indochine.* 1936. Apr. Vol. 6. No. 23. pp. 393–401.

[27]JAKEMAN (Harry W.). Some Phases of Rabies and Distemper Control.—*Jl. Amer. Vet. Med. Assoc.* 1937. Apr. Vol. 90. No. 4. pp. 493–500.

[28]WEBSTER (Leslie T.). Diagnostic and Immunological Tests of Rabies in Mice.—*Amer. Jl. Public Health.* 1936. Dec. Vol. 26. No. 12. pp. 1207–1210. With 3 figs.

to rabies than other laboratory animals per gram of body weight." " One-hundred-millionth gm. of mouse brain virus is fatal to at least 50 per cent. of these mice when injected intracerebrally, the intramuscular and subcutaneous dosage is 1/10,000 gm." Mouse protection tests have been employed in various directions. A serum protection test was employed to measure the amount of neutralizing antibodies in mice following experimental vaccination. In one series of tests sera of persons treated with vaccines containing live virus were found to neutralize 100 to 1000 lethal doses over periods as long as 4 years. One Semple vaccine (G) treatment remained effective (neutralized 100 doses) up to 15 months. A second Semple vaccine (N) however had no effect.

Resistance tests were also carried out. " Results thus far suggest, from the theoretical view-point, that neutralizing antibodies are not always a direct measure of resistance, and that vaccines containing no demonstrable living virus may produce resistance. Moreover, they show that the optimum method of securing prompt and effective immunity to rabies in the mouse is by the intraperitoneal injection of relatively large amounts of vaccine, 6 doses, one every other day."

vi. *Miscellaneous.*

Levaditi, Schoen and Reinié[29] continue their researches on negrigenesis in tumour cells. It will be remembered that this occurred in the case of Pearce's carcinoma (this *Bulletin*, 1936, Vol. 33, p. 750). In a couple of experiments on rabbits suffering from Shope's papilloma, the tumour cells were much less affected : some oxyphil bodies of doubtful nature were seen, and one out of 9 rabbits inoculated with tumour tissue became infected. Thus the affinity towards different neoplasms varies considerably. It depends not only on the nature of the neoplasms (ectodermic or mesodermic), but also on their proliferative capacity.

A later paper[30] gives a continuation of the research already referred to (this *Bulletin*, 1936, Vol. 33, p. 750) on negrigenesis in Pearce's carcinoma. Street virus Rabies has been transmitted through 9 subpassages, by simple implantation of infected tumour tissue into the anterior chamber of the eye. Typical Negri bodies are seen in the tumour cells. They are more numerous in the older corneal cells close to Descemet's membrane than in those of the deeper layers. Using fixed virus it was not possible to obtain subpassages with regularity, as was the case with street virus. Thus the virus of rabies appears to have an affinity for embryonic tissue, and in the state of " street virus " it can in embryonic tissue go through the complete cycle of its evolution.

Haguenau, Cruveilhier and Viala[31] find that the action of antirabic vaccine during the period of lactation leads to the regression

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[29]Levaditi (C.), Schoen (R.) & Reinié (L.). Virus rabique des rues et papillome de Shope.—*C. R. Soc. Biol.* 1937. Vol. 124. No. 9. pp. 793–794.

[30]Levaditi (C.), Schoen (R.) & Reinié (L.). Virus rabique et cellules néoplasiques.—*Ann. Inst. Pasteur.* 1937. Apr. Vol. 58. No. 4. pp. 353–376. With 13 figs.

[31]Haguenau (J.), Cruveilhier (L.) & Viala (C.). Effets de l'action conjuguée du virus rabique et de la lactation sur la tumeur de Shopes du lapin.—*C. R. Soc. Biol.* 1937. Vol. 124. No. 10. pp. 892–893.

of SHOPE's carcinoma in the rabbit. On the other hand, neither antirabic vaccine alone, nor lactation alone, nor normal brain substance associated with lactation have any effect. The regression was complete when lactation was complete, and partial when lactation was partial.

A case of poliomyelitis acuta in which there was a previous history of the patient having been bitten by a dog, has been investigated by VELDE[32]. After a discussion of the literature relating to somewhat similar cases, he concludes that in the case under review there is little evidence of any direct relation between the bite and the poliomyelitis.

A. G. McKendrick.

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[32]VELDE (G.). Poliomyelitis acuta und Hundebiss.—*Med. Klin.* 1936. Dec. 4. Vol. 32. No. 49. pp. 1667–1669.

YELLOW FEVER.

Boletín de la Oficina Sanitaria Panamericana. 1936. Aug. Vol. 15. No. 8. pp. 744–751. [11 refs.]—El estado actual del problema de la fiebre amarilla. [**The Present State of the Yellow Fever Problem.**]

This article, prepared by the Yellow Fever Service of Brazil, with the assistance of the Rockefeller Foundation, adequately sums up present-day knowledge of yellow fever. It is intended as a summary and therefore contains nothing new. The points on which stress is laid are :—

1. Ordinary urban yellow fever being transmitted by *Aëdes aegypti* is controllable by anti-mosquito (including anti-larval) measures.
2. Selvatic yellow fever occurs independently of *Aëdes*, assumes epidemic proportions in Southern Brazil, Bolivia and eastern Colombia and is sporadic in Magdalena and the Amazon Valley.
3. Selvatic or jungle yellow fever attacks those individuals only who enter or work in the woods.
4. Examinations of portions of liver removed from bodies with the viscerotome is the best method of diagnosis after death, and the protection test with the serum of suspected cases the best in life.
5. Vaccination probably affords the best protection against selvatic yellow fever.
6. Captured monkeys show a natural immunity to infection with virus, but we do not yet know either the animal hosts, the vectors, or the way in which the infection traverses large tracts of forest.

H. H. S.

Sawyer (Wilbur A.), Bauer (Johannes H.) & Whitman (Loring). **The Distribution of Yellow Fever Immunity in North America, Central America, the West Indies, Europe, Asia, and Australia, with Special Reference to the Specificity of the Protection Test.**—*Amer. Jl. Trop. Med.* 1937. Mar. Vol. 17. No. 2. pp. 137–161. With 3 maps. [24 refs.]

A valuable summary of earlier investigations on the distribution of yellow fever immunity together with the authors' final report on surveys in all countries outside of Africa and South America. The specificity of the yellow fever protection test in mice is dealt with in detail and it is shown that out of 876 human sera from Asia and Australia, where presumably the disease has never been present, only 2 specimens showed protection against yellow fever virus. Among 481 sera from Italy, Spain, Portugal, Canada and the U.S.A., where the disease was formerly present but is now absent, only one was protective. The nature of these odd cases showing non-specific virucidal substances in the blood is very obscure, and the blood of one of them was tested against two other viruses, but possessed no protective properties against either. The blood of this particular subject, a Tamil who had never been out of India, protected mice against 10 per cent. yellow fever, virus-brain suspension, even when the serum was diluted 1 : 10, and these protective properties lasted for at least 3 years. It would appear, therefore, that occasionally,

but only very rarely, yellow fever virucidal substances may be present in the serum of persons who have never been exposed to infection.

A total of 1,177 sera were tested from various islands in the West Indies: Barbados, Cuba, Jamaica, Porto Rico, St. Lucia and Trinidad. The 821 sera from persons under 20 years of age were all negative, but of the remaining 356, 20 years or older, 30, or 8·42 per cent., gave positive protection tests.

A total of 1,089 sera from Mexico gave the following results:—

Age group of donors	No. tested	No. positive	Percentage positive
5–9 years	321	3	0·90
10–14 years	386	33	8·55
15–19 ,, ...	59	17	28·81
20 years and over	323	138	42·72

All sera from children born after 1925 gave negative results, so the disease has probably now disappeared from Mexico.

A total of 1,182 specimens from the 7 Central American countries gave very similar results for El Salvador, Guatemala, British Honduras, Honduras and Nicaragua, but in the case of Panama and Costa Rica the disease seems to have been absent for a longer time, as the sera of all persons under 20 years were negative. *E. Hindle.*

Sudan Medical Service Report for the Year 1935 [Pridie (E. D.), Director]. [**Yellow Fever** pp. 74–75.]

Survey work in yellow fever was continued in the Sudan in two directions: 1. Examination of liver tissue obtained by viscerotome from as many patients as possible who died in 8–9 days with jaundice or a history of fever of unknown origin. 2. Collection of sera for mouse-protection tests.

Under the former 30 specimens were received; 29 were negative. The other was from a man of 25 years of age with symptoms suggestive of yellow fever. He arrived at Malakal after a journey of four days from Liri Nuba and was taken ill 16 days afterwards with epigastric pain and vomiting. Three days later he was intensely jaundiced and comatose. There was no history of any fever, nor was there any while he was in hospital. He died on the third day after admission, *i.e.*, after an illness of 6 days. The slide was sent to Dr. G. M. Findlay, who thought the changes extraordinarily suggestive of yellow fever, but the history of early jaundice and the absence of fever were strong points on the other side.

Under the second, sera from 29 patients were sent to London. Nine gave protection by the mouse test, 8 from Southern Sudan and one from Wad Medani.

In this connexion attention must be directed to the peculiar syndrome of moderate fever, deep jaundice and vomiting with albuminuria which has been observed in the Sudan for the past two years or more. Some cases end fatally; mouse protection tests give negative results and there is marked liver necrosis. This condition bears a strong resemblance to " an obscure infective disease associated with jaundice "

reported from Nigeria in 1931. [See this *Bulletin*, 1931, Vol. 28, p. 858 ; if the reviewer recollects aright, this disease was 'epidemic' in Nigeria, but that it was 'infective' was not proved.] *H. H. S.*

PELTIER (M.). Les fièvres de nature indéterminée dans les colonies françaises. [**Fevers of Uncertain Nature in the French Colonies.**]—*Ann. de Méd et de Pharm. Colon.* 1936. Apr.–May–June. Vol. 34. No. 2. pp. 215–235. [38 refs.]

Among the febrile conditions referred to in this article are some about which there is little doubt, such as dengue, pappataci fever, typhus, Weil's disease, but others mentioned certainly call for further investigation : Thus the *Inflammatory* or *Antilles fever*, with abrupt onset, temperature 40°–41°C., severe headache, injected conjunctiva, lasting 4 or 5 days, then, after a brief remission, a return of fever with gastric symptoms ; albuminuria is present but not marked and is a transient sign only. The author knows of no case of true yellow fever occurring from *Aëdes* biting a patient with "inflammatory fever," but the description is very suggestive of mild yellow fever. The mouse protection test ought, of course, to be made.

Again, the *Black Vomit of Guadeloupe* would seem to leave no doubt of being yellow fever, but its attacks are almost confined to children, during the period March–June, and Creole children, not Europeans, and one attack does not confer immunity. Some think it is malaria, but plasmodia are not found in the blood and quinine is ineffectual.

In the terminal quarter of 1932 an epidemic raged in Labé, Koumbia and Boké (French Guinea) with high fatality. In Labé there are said to have been 5,000 cases, 1,000 deaths ; in Koumbia 3,000 cases, 500 deaths ; in Boké 600 cases, 40 deaths [the round figures make one suspicious of the accuracy of these returns], altogether 8,600 cases, 1,540 deaths, a 17·9 per cent. fatality. The symptoms were sudden onset of fever with headache, profuse epistaxis, serous diarrhoea, sometimes vomiting, jaundice, usually slight but persisting, no pulmonary complications ; death occurred or recovery began to set in on the 12th to 14th day.

Other febrile conditions referred to are dioundé [see this *Bulletin*, 1933, Vol. 30, p. 719] and *fièvre rouge* of the Congo [this *Bulletin*, 1932, Vol. 29, pp. 454, 795 ; 1935, Vol. 32, p. 171]. *H. H. S.*

BENARROCH (E. I.). La fiebre amarilla de Guayana en 1929. [**Yellow Fever in Guayana (Venezuela) in 1929.**]—*Gac. Méd. de Caracas.* 1936. Jan. 31. Vol. 43. No. 2. pp. 19–22. With 3 charts.

The last outbreaks of yellow fever in Venezuela were recorded in Coro (1918), Maracaibo (1917), Maracay (1914) and Caracas (1912). That referred to in the present paper started at El Callao towards the end of June 1928. The total of cases numbered between 250 and 300, of which 15 ended fatally, and the outbreak terminated in April 1929. Those seen by the author occurred in Guasipati, a locality with about 1,500 inhabitants. A typical and fatal case took place in March 1929. The disease began with fever 38·5°–39·5°C., a remission to 37·5°C. on the third day when also jaundice was first noticed. Vomiting was at first bilious, then dark brown and later bloody. There was severe pain in the head, back and epigastrium. Between the 15th March and 31st May 149 cases occurred and 5 patients died—

a low fatality rate. The distribution by age was : 1–9 years 27 cases, 2 severe ; 10–19 years 70 cases and 4 fatal ; 20–29 years 31 cases ; 30–39 years 12 ; 40 years and over, 9 cases. The outbreak was essentially a " domestic " one ; the house *Aëdes* larva index was 100 per cent., and adults 80 per cent. The diagnosis was confirmed by autopsy, histological examination of tissues and by serological tests carried out by investigators of the Rockefeller Foundation. *H. H. S.*

Carvallo (T.). Conceptos sobre fiebre amarilla e inmigración. [**Observations on Yellow Fever and Immigration.**]—*Gac. Méd. de Caracas.* 1936. Jan. 31. Vol. 43. No. 2. pp. 22–25.

Remarks of a general character on immigration and the introduction and disappearance of yellow fever, instigated and based upon Benarroch's paper above. *H. H. S.*

Stock (P. G.). Une épidémie de fièvre jaune survenue en mer sur un navire.—*Procès-Verb. Comité Permanent de l'Office Int. Hyg. Publ. Séssion ordinaire d'Oct., 1936.* pp. 53–56.

Public Health Reports. 1937. Mar. 19. Vol. 52. No. 12. pp. 336–337.—**Yellow Fever on Shipboard.**

An interesting account of an outbreak of yellow fever on board a steamer travelling between Dakar, French West Africa and the River Tyne, England, during which there were 14 cases of severe illness with 7 deaths, among a crew of 24.

The ship spent 8 days loading cargo at Kaolakh and Zighinchor (July 31st to August 7th, 1936) and sailed from Dakar on August 9th. Between August 13th and 19th, 14 of the officers and crew became ill, and at Madeira this illness was diagnosed as food poisoning. On arrival in England 7 members of the original crew had died with symptoms, including intense jaundice, strongly suggestive of yellow fever, 5 were in hospital at Madeira, and 2 had been ill but remained on duty. In view of the possibility of yellow fever, protection tests were made with samples of blood from members of the crew, some of them new hands engaged to replace the sick, and of 14 samples examined, 6 gave a positive reaction, including 4 from men who had been hospitalized in Madeira and 2 from the men who had been ill but remained on duty ; none of the 8 negative had shown any symptoms of illness. *E. H.*

Galvão (A. Ayroza) & Lane (John). Notas sobre mosquitos de Juquiá (Estado de S. Paulo). [**On Mosquitoes of Juquiá, S. Paulo.**] —Reprinted from *Rev. Biol. e Hyg.* 1935. Dec. Vol. 6. No. 2. pp. 113–120. With 8 figs.

In November 1935 the authors visited Poço Grande, about 10 kilometres distant from S. Antonio do Juquiá, and 80 metres above sea level. They made a collection of mosquitoes which appear to be fairly abundant there ; they caught approximately 2,000 in 3 hours. Among them were *Aëdes* belonging to two groups, *fulvus* and *scapularis* ; Psorophora and Janthinosoma. Of the first were the following species : *nubilus, serratus, fulvus* ; of the second, *crinifer* and *leucomelas*. Their interest for human medicine lies in their possible capabilities as vectors of the yellow fever virus.

H. H. S.

Komp (W. H. W.). An Annotated List of the Mosquitoes found in the Vicinity of an Endemic Focus of Yellow Fever in the Republic of Colombia.—Reprinted from *Proc. Entom. Soc. Washington.* 1936. Apr. Vol. 38. No. 4. pp. 57–70. [17 refs.]

Burke (A. W.). **An Epidemic of Jungle Yellow Fever on the Planalto of Matto Grosso, Brazil.**—*Amer. Jl. Trop. Med.* 1937. May. Vol. 17. No. 3. pp. 313–314. With 2 maps & 1 fig. [17 refs.]

A detailed account of an epidemic of 201 cases of yellow fever of the jungle type, without *Aëdes aegypti*, on the Planalto of Matto Grosso, Brazil, during 1934 and 1935.

The identity of the disease was established by clinical observation, autopsy, protection test, and the transfer of infection from early human cases direct to white mice. In 15 cases negative protection tests were obtained before the onset of the illness, or early in the course of the disease, followed by positive protection tests with the convalescent sera.

A protection test survey gave results supporting the view that the outbreak was probably part of Amazonian jungle endemicity. Thus the examination of 94 inhabitants of the town Coronel Ponce gave only 7·5 per cent. positive ; 150 persons from houses more than 3 km. from fields and jungle gave 16·7 per cent. positive ; whilst 430 from houses less than 3 km. from fields and jungle gave 39·3 per cent. positive.

The paucity of the human population in the infected district and the scatter of cases both in time and space, together with the isolated circumstances attending many of the cases, argue against man being the only vertebrate host involved. Moreover, the sera from 5 *Cebus* monkeys caught in known infected districts all gave positive protection tests.

All available evidence points to the infection occurring either in clearings next to the jungle, or in the jungle itself, the rural rates of infection rising as the proximity of the house to fields and jungle increases.

The vector or vectors of yellow fever in this region present an interesting problem, and in view of the occurrence of jungle yellow fever in Brazil, Bolivia and Colombia, under widely different conditions, more than one carrier may be involved. *E. H.*

Aragão (Henrique de Beaurepaire). Transmissão da febre amarella sylvestre pelo stegomyia (*Aedes egypti*) e pelos mosquitos da Matta.—*Brasil-Medico.* 1937. Apr. 24. Vol. 51. No. 17. pp. 497–499.

Chowdhury (K. L.) & Ganguli (A. C.). **The Problem of the Control of Stegomyia Mosquitoes in Calcutta with Special Reference to Yellow Fever and Dengue. With Appendix A & B.**—*Jl. Indian Med. Assoc.* 1937. May. Vol. 6. No. 8. pp. 421–426. With 1 map & 2 charts. [23 refs.]

The record of a *Stegomyia* survey undertaken in Calcutta in view of the increased danger of importation of yellow fever by aerial traffic.

The percentage of houses infested with larvae was 12·6, *Aëdes aegypti* being the commonest species, followed by *A. albopictus*. Dengue is common in Calcutta and in heavy epidemics may affect 30–40 per cent. of the population, therefore favourable conditions

obviously exist for the spread of yellow fever. The main breeding places were found to be rain-water collected in unserviceable articles and water-storage cisterns, which together were responsible for 82 per cent. of the 2,312 breeding places examined. Continuous water supply at high pressure and a thorough house-to-house inspection once a week are considered necessary for control.

Appendix A by Dr. M. T. MORGAN comprises notes on a tour of inspection of the Co-operative Anti-yellow Fever Service in Brazil. [see this *Bulletin*, 1935, Vol. 32, p. 585].

Appendix B gives particulars of the Notification of the Government of India *re* Yellow Fever Menace.

" 'In exercise of the power conferred by section 2 of the Epidemic Diseases Act, 1897 (III of 1897) the Governor-General-in-Council being satisfied that India is threatened with an outbreak of yellow fever, is pleased to direct (1) that no person shall arrive in India by an aircraft, within nine days of his being in an area in which yellow fever exists, or in which, though the disease has not been clinically demonstrated, there is presumptive evidence, as a result of mouse protection tests, that the disease has occurred in that area, unless he has been protected by satisfactory inoculation, or previous attack of the disease, and (2) that no aircraft, which started from or alighted in any such area, shall enter India.' "

E. H.

PUBLIC HEALTH REPORTS. 1937. May 21. Vol. 52. No. 21. pp. 671–672.—**Airplane Company Institutes Measures against Yellow Fever.**

A report that Pan American Airways, Inc. has instituted the following control measures in view of the possibility of infected mosquitoes being introduced from South America.

" 1. All flying personnel not already vaccinated against yellow fever will be vaccinated here in Rio de Janeiro at the Rockefeller laboratory. This will be begun at once, and will be finished as soon as may be possible. The flying personnel will include aviators, radio operators, flying mechanics, pursers, stewards, etc.

" 2. Beginning May 1, 1937, cards will be filled out for all passengers which will show where they have been or have resided for the six (6) days just prior to embarking en route to the United States. These cards will be attached to the passenger list of the airplane and will be available to the Quarantine Officer on arrival at destination."

A worthy example of co-operation between an Air-Line and the Public Health Service!

E. H.

SOPER (Fred L.). **The Newer Epidemiology of Yellow Fever.**—*Amer. Jl. Public Health.* 1937. Jan. Vol. 27. No. 1. pp. 1–14. [24 refs.]

A general summary of recent observations on the epidemiology of yellow fever, with special reference to observations in South America, and the existence of a " jungle type " of the disease. This differs from the classical type, in that it occurs in the absence of *Aëdes aegypti*, and persists in rural districts under conditions previously considered incompatible with yellow fever endemicity.

This jungle yellow fever, in the absence of adequate methods for its control, must be considered as a possible permanent source of the

virus for the reinfection of towns where high densities of *Aëdes aegypti* are tolerated. *E. H.*

RICKARD (E. R.). **The Organization of the Viscerotome Service of the Brazilian Cooperative Yellow Fever Service.**—*Amer. Jl. Trop. Med.* 1937. Mar. Vol. 17. No. 2. pp. 163–190. With 7 figs.

A detailed account of the administrative procedure of the "Viscerotome Service" in Brazil, the success of which has depended mainly upon the proper selection and instruction of representatives who are to obtain specimens, the full application of existing legislation in regard to the registry of deaths, and the burial of bodies, making provision for representatives *faire viser* all death certificates before burial can take place, the legalization by executive decree of obligatory viscerotomy, and especially frequent visits to representatives by Service medical personnel, resulting in the maintenance of close contact between the Service offices and the representatives.

The article should be consulted in the original by all those interested in the subject as the author goes into details of the many difficulties that may be encountered and means of dealing with them in order to ensure the success of this method of investigation. *E. H.*

DEZEST (G.). Un cas de réaction nerveuse grave après vaccination antiamarile. Auto-observation. [**A Case of a Serious Nervous Reaction after Yellow Fever Vaccination. Auto-Observation.**]—*Bull. Soc. Path. Exot.* 1937. Apr. 14. Vol. 30. No. 4. pp. 253–257.

The author, a medical officer with the French Colonial Troops, describes the severe nervous symptoms which developed 8 days after he had received an inoculation of yellow fever vaccine [type not stated].

There was not the slightest reaction after the injection, but 8 days later a suborbital headache developed, and the aches gradually extended down the spinal column, becoming easier after about 48 hours. For the next 16 days there were sudden attacks of lumbar pains of short duration. Then the symptoms became more acute and were accompanied by the development of fever, which did not respond to aspirin, and 32 days after the inoculation it was necessary to stay in bed, and in the succeeding days the patient became delirious, with a high fever, albuminuria, low blood pressure, and finally slight jaundice of the conjunctivae and palms of the hands. The temperature dropped after 10 days, and the patient recovered his mental faculties about 8 days later. One month later some of the peripheral muscles of the right hand were found to be infected. The serum tested by Dr. Stéfanopoulo was found to protect mice up to dilutions of 1 : 1000.

E. H.

SAWYER (W. A.). **Experience in vaccinating against Yellow Fever with Immune Human Serum and Virus fixed for Mice.**—*Amer. Jl. Hyg.* 1937. Mar. Vol. 25. No. 2. pp. 221-231. With 1 fig. [13 refs.]

The author gives a final report on yellow fever vaccination by means of immune human serum and dried living yellow fever virus fixed for

mice, which is being replaced by the use of a modified virus strain of very low virulence without injecting immune serum.

Out of the 88 persons vaccinated in the Laboratories of the International Health Division of the Rockefeller Foundation in New York, through subcutaneous injections of virus and immune serum, the protective antibody content of the blood was followed in 45 for lengths of time up to 4 years. The mean protective titres of the blood shows that antibodies appear about one week after vaccination, reach a maximum after about 6 weeks, remain at this level for 2½ months and then gradually fall. Some sera tested after 3 and 4 years were still protective, but others had lost all power to protect after 2 years. It was concluded that blood should be examined every 2 or 3 years, and persons revaccinated if their blood had lost its protective power. Revaccination is safe and effective, but the results are not so lasting as those of the first vaccination.

Details are given of an attack of probable encephalitis which came on late in one of the vaccinated persons after humoral immunity against yellow fever had been thoroughly established. The human serum and virus used in his vaccination had been used in the immunization of 7 other persons without any unusual effects. The author reviews various possibilities, including that of some other filterable virus accidentally present in the mouse brain, but the case is not satisfactorily explained. However, it has been a stimulus in the effort to diminish the neurotropism of the virus used and to cultivate it in fowl embryo tissue *in vitro* instead of in mouse brain *in vivo*. *E. H.*

Laigret (J.), Durand (R.) & Bonneau (E.). Enquête sérologique dans un régiment de tirailleurs sénégalais pour le dépistage des atteintes anciennes de fièvre jaune. [**A Serological Study of a Regiment of Senegalese Tirailleurs in order to determine Previous Infection with Yellow Fever.**]—*Bull. Soc. Path. Exot.* 1937. May 12. Vol. 30. No. 5. pp. 341–343.

The sera of 100 Senegalese soldiers from various French African colonies have been examined by means of the mouse-protection test and the results confirm the view that yellow fever is very widespread as indicated in the following list :—

Country	No. of Sera Tested	Positive	Negative	Doubtful
French Sudan	15	9	5	1
Dahomey	15	5	7	3
Ivory Coast	18	2	14	2
Upper Volta	14	5	6	3
French Guinea	21	7	13	1
Senegal	9	5	3	1
Niger Territory ...	7	2	5	—
Tchad	1	—	1	—

In view of the fact that one-third of the natives of military age have already had yellow fever, the authors advocate the general vaccination of school-children, using coated vaccine. *E. H.*

Sellards (A. W.) & Laigret (Jean). Preuves de l'immunité acquise contre la fièvre jaune à la suite de sa vaccination. [**Evidence of Immunity against Yellow Fever acquired after Vaccination.**]—*Arch. Inst. Pasteur de Tunis.* 1936. Nov. Vol. 25. No. 3 & 4. pp. 424–436.

The authors state that in Africa during the past three years, about 20,000 persons have been vaccinated against yellow fever, most of them in endemic areas, and not a single case of the disease had occurred in any of these subjects.

Details are given of protection tests in mice and monkeys with the serum of subjects before and after vaccination showing the development of antibodies, and particulars are given of one individual who in addition to the foregoing tests was exposed to the bites of infected *Aëdes aegypti* seven months later. The patient was unaffected by this exposure to infection, whilst two *rhesus* monkeys bitten by the same lot of mosquitoes both died of yellow fever. *E. H.*

Laigret (J.), Saleun (G.) & Ceccaldi (J.). Enquête sérologique sur dix-neuf sujets immunisés contre la fièvre jaune, les uns à l'aide de la vaccination, les autres à l'aide de la séro-vaccination. [**A Serological Inquiry on 19 Subjects Immunized against Yellow Fever, Some by Means of Vaccination, Others by Means of Serum-Vaccination.**]—*Bull. Soc. Path. Exot.* 1937. Jan. 13. Vol. 30. No. 1. pp. 8–10.

By means of intracerebral tests in mice the authors have compared the immune titre of 9 subjects vaccinated about 1 to 2 years previously by the inoculation of virus alone, with that of 10 subjects inoculated with virus and immune serum, on the average about one year previously. Although considerable individual variations are shown, the immune titres of the former are much higher than in the case of those receiving both virus and immune serum. It is of interest that in one of the first and three of the second group of those vaccinated, the protective properties of the blood had completely disappeared. Four patients vaccinated by virus alone showed titres of 25,600 units per cc., whilst only 3 of those inoculated with virus and immune serum showed titres as high as 640 units per cc. *E. H.*

Mathis (C.), Durieux (C.) & Mathis (M.). Est-il prudent de se faire vacciner contre la fièvre jaune en Afrique Occidentale Française. [**Is it wise to be vaccinated against Yellow Fever in French West Africa ?**]—*Bull. Soc. Path. Exot.* 1936. Dec. 9. Vol. 29. No. 10. pp. 1042–1046.

The authors show that there were 113 deaths from yellow fever in French West Africa during 1931 to 1935 inclusive, among a total white population of 27,220. Excluding the Dakar population of 10,000, where the absence of mosquitoes eliminates the risk of infection, and taking the average tour of duty as 2 years, it is estimated that during this period there is a 1 in 400 chance for each person of succumbing to the disease.

At the Pasteur Institute, Dakar, 600 inoculations have been effected without any serious accidents, but post-vaccinal reactions may occur. Details are given of the clinical histories of four young

doctors, each of whom received on the same day similar doses of the same batch of vaccine. One showed no post-vaccinal reactions, the second a slight reaction, the third a moderate one, and the fourth a prolonged reaction with symptoms lasting for about 3 weeks. The latter case, however, which must be regarded as exceptional, recovered completely without showing any after effects and his blood 6 weeks later was found to be strongly protective in mice. *E. H.*

Findlay (G. M.) & MacCallum (F. O.). **An Interference Phenomenon in Relation to Yellow Fever and Other Viruses.**—*Jl. Path. & Bact.* 1937. Mar. Vol. 44. No. 2. pp. 405–424. [35 refs.]

The authors have studied Hoskin's observation (see this *Bulletin*, 1936, Vol. 33, p. 341) that monkeys inoculated with a mixture of pantropic and neurotropic virus survive, whilst control monkeys inoculated with the pantropic virus alone succumb. When the neurotropic virus is inoculated 24 hours after the pantropic virus there is no protection. The intracerebral inoculation of 4 monkeys with this mixture resulted in death from encephalomyelitis, whilst 2 control monkeys inoculated intracerebrally with pantropic virus alone died with liver necrosis and other visceral lesions. Similarly, 7 out of 8 hedgehogs inoculated subcutaneously with the mixture died of encephalitis, whilst those inoculated with only pantropic virus died with liver necrosis and gastric haemorrhage. In mice inoculated intracerebrally with mixtures of the two viruses death is dependent on the neurotropic virus ; the pantropic virus does not afford any protection against it.

The subcutaneous inoculation of 16 human beings with mixtures of the two viruses and yellow fever immune serum gave reactions similar to those induced by the neurotropic virus.

The evidence supports the view that neurotropic protects against the pantropic virus, but the latter does not protect against the neurotropic virus. This action is not due to any precocious development of immune bodies, and therefore tests were made to see if the blocking of certain cells by one virus interfered with the activity of a second virus, as in the case of certain plant viruses.

Accordingly, monkeys and mice were inoculated with mixtures of yellow fever virus and Rift Valley fever virus, and a well marked interference was obtained. Thus the inoculation of a mixture resulted in the protection of 7 out of 11 monkeys. In mice the intraperitoneal inoculation of a mixture of neurotropic yellow fever virus and pantropic Rift Valley fever virus caused a delay in the death of the mice and 6 out of 60 survived. This protective action was not seen if the Rift Valley fever virus was given 24 hours before the inoculation of yellow fever virus. No protective action against Rift Valley fever virus in mice was shown by intraperitoneal inoculation of normal mouse brain, mouse brain containing killed neurotropic virus, or India ink ; and a scarcely perceptible protection by a strain of fowl pest virus, non-pathogenic for mice.

The above phenomena suggest that there may be a generic relationship between yellow fever and Rift Valley fever, which is not apparent by the ordinary tests, but shown by interference phenomena, and in this connexion the geographical distribution of the two diseases is of interest. Yellow fever is predominantly West African and has

never reached Kenya and the East Coast, whilst Rift Valley fever occurs in Kenya, Uganda, French Equatorial Africa, etc., but not in Nigeria or other West African Colonies. *E. H.*

THEILER (Max) & SMITH (Hugh H.). **The Effect of Prolonged Cultivation in Vitro upon the Pathogenicity of Yellow Fever Virus.**—*Jl. Experim. Med.* 1937. June 1. Vol. 65. No. 6. pp. 767–786. [16 refs.]

A valuable report on the changes that have taken place in yellow fever virus in the course of continual cultivation *in vitro* for a period of more than three years without any intervening passage through a living host.

The three strains of virus used in these experiments were all derived from the same original virus, the well-known and extremely virulent Asibi strain. In the tissue cultures one strain was propagated on whole mouse-embryo, another on fowl-embryo from which the head and spinal cord had been removed, and the other on testicular tissues of mice and guineapigs. The changes in pathogenicity of the virus cultivated for 240 subcultures during a period of more than three years in a medium containing whole mouse-embryo were not striking. The viscerotropic virulence seemed to be somewhat diminished, as it failed to produce fatal infections when inoculated subcutaneously into rhesus monkeys or hedgehogs, but a generalized infection takes place accompanied by a relatively high concentration of virus in the circulating blood. The neurotropic virulence of the strain remained unchanged.

The changes in pathogenicity of the strain cultivated in a medium containing fowl-embryo tissues from which the head and spinal cord had been removed were most pronounced. The viscerotropic virulence of the virus was so reduced that when inoculated into monkeys only a mild generalized infection resulted, with minimal quantities of virus in the circulating blood. Probably as a result of the absence or scarcity of nervous tissue in the culture medium the neurotropism of the virus was also much diminished, and when inoculated intracerebrally into monkeys produced only a moderate febrile reaction followed by recovery and solid immunity. This change had a comparatively sudden onset, for at the 89th subculture the strain was highly neurotropic for monkeys, and still produced visceral infections with abundance of virus in the blood, but in the 114th subculture had lost both these properties. When injected intracerebrally into mice the mortality ratio was not diminished, but the time interval between inoculation and death was prolonged from an average of about 7 days at the 114th subculture to one of 9·8 days at the 176th subculture.

The changes in the pathogenicity of the strain cultivated for more than 160 subcultures in a medium containing testicular tissues were somewhat similar to those occurring in fowl-embryo tissue containing minimal amounts of nervous tissue. The viscerotropic properties were very reduced and only minimal quantities of virus appeared in the blood circulation of inoculated monkeys. When given intracerebrally, however, it produced death from encephalitis in monkeys. In mice the incubation period was also prolonged, but somewhat less so than in the case of the virus grown in fowl-embryo tissues without the central nervous system. *E. H.*

Theiler (Max) & Smith (Hugh H.). **The Use of Yellow Fever Virus modified by in Vitro Cultivation for Human Immunization.**—*Jl. Experim. Med.* 1937. June 1. Vol. 65. No. 6. pp. 787–800. [13 refs.]

The authors give details of the results of inoculating into monkeys varying amounts of the culture virus referred to above which had been grown in fowl-embryo tissue containing minimal quantities of nervous tissue.

The results indicate that the anti-body titre developed in monkeys bears no relation to the dose. Within 7 days monkeys inoculated subcutaneously with this tissue-culture virus are rendered immune to a subsequent injection of highly virulent yellow fever virus.

Four immune human subjects were inoculated with the culture virus and all showed a marked rise in antibodies; apart from a slight local reaction at the site of injection, no other symptoms were noticed. The antibody titre reached its maximum about the 4th to the 8th week and then slowly declined.

Eight normal persons have been vaccinated with this culture virus from the 227th and 229th subcultures. Five persons had a slight febrile reaction, with one exception between the 5th and 7th days, accompanied by slight headache and backache. Antibodies were present in the blood two weeks after vaccination, and in the case of two subjects examined at intervals, the titre was found to rise up to the 4th week but remained very low. The results are sufficiently encouraging to warrant a more extensive trial of the method.

E. H.

Smith (Hugh H.) & Theiler (Max). **The Adaptation of Unmodified Strains of Yellow Fever Virus to Cultivation in Vitro.**—*Jl. Experim. Med.* 1937. June 1. Vol. 65. No. 6. pp. 801–808.

At first the authors without success made many attempts to cultivate four unmodified strains of yellow fever virus, using the technique employed by Haagen and Theiler for the Asibi strain [see this *Bulletin*, 1932, Vol. 29, p. 577]. Subsequently mouse embryos, about the 13th day of pregnancy, were inoculated with the virus *in utero* and a titration taken of the virus content of the different organs of the embryos. The results showed that the virus was present in the brain in greatest concentration.

Accordingly a medium was prepared consisting of minced mouse-embryo brain tissue and Tyrode solution containing 10 per cent. normal monkey serum. In this tissue unmodified strains of yellow fever virus were readily adapted to cultivation *in vitro*, including seven different strains ranging in pathogenicity from the highly virulent French strain to the recently isolated viruses from " Jungle Yellow Fever " which are low in both neurotropic and viscerotropic properties. Subcultures in mouse-embryo brain tissue medium were made at 3 to 5 day intervals, and after 20 to 25 subcultures the strains were readily adapted to cultivation in whole mouse-embryo tissue medium.

The prolonged cultivation of the virus in this brain tissue medium seems to have no effect on the neurotropic properties of the virus.

E. H.

Jadin (J.). Culture du virus de la fièvre jaune sur la membrane chorio-allantoidienne de l'embryon de poulet. [**The Culture of Yellow Fever Virus on the Chorio-Allantoic Membrane of the Fowl Embryo.**]—*Ann. Soc. Belge de Méd. Trop.* 1937. Mar. 31. Vol. 17. No. 1. pp. 27–32.

After 6 to 7 days incubation fowls' eggs were inoculated with brain emulsions of mice infected with yellow fever, and after 4 or 5 days further incubation subsequently examined for the presence of virus. The results show that the virus multiplies in the tissues of the embryo and also extends into the surrounding albumen. Although in most cases the eggs were examined four or five days after inoculation, the virus was found to persist in the embryo up to the 18th day of incubation, but a chick of the same batch which was allowed to hatch contained no trace of virus.

The properties of the virus remained unaffected by culture in fowl embryos, and this would seem to be a very simple and practicable method of maintaining yellow fever virus. *E. H.*

Elmendorf (John E.), Jr. & Smith (Hugh H.). **Multiplication of Yellow Fever Virus in the Developing Chick Embryo.**—*Proc. Soc. Experim. Biol. & Med.* 1937. Mar. Vol. 36. No. 2. pp. 171–174.

An independent account of the use of developing fowl embryos for the cultivation of yellow fever virus. The authors obtained similar results to those recorded by Jadin, but have simplified the technique of egg passage by inoculating the virus suspension directly into the embryo as seen by transmitted light.

Various strains of virus were successfully maintained in developing eggs. Sixty consecutive passages were made with a culture strain adapted to fowl embryo tissue, the optimum age of the incubated eggs being 7 to 8 days. The intervals between transfers varied from 2 to 8 days.

A strain adapted to mouse embryo tissue was also used and a similar multiplication of virus observed in the developing fowl embryos.

Four viscerotropic strains, two highly pathogenic ones from Africa and two from Brazil with only a mild degree of virulence, were successfully cultivated in this manner, but these unmodified strains were not so readily adapted to growth in the developing fowl embryo and in three cases repeated attempts were made before being successful. Once the strain had been carried through 2 or 3 passages no difficulty was encountered in continuing its propagation in this manner.

In one test a monkey inoculated with the French virus after 10 egg-to-egg passages died of typical yellow fever, showing there had been no modification in the virulence of the virus. In another test a culture strain, after 165 subcultures in fowl embryo tissue and 18 serial egg-to-egg passages, was inoculated into 4 monkeys, all of which developed protective antibodies against yellow fever. *E. H.*

Findlay (G. M.) & MacCallum (F. O.). **Attenuation of the Yellow Fever Virus by Growth in Tumours** *in Vivo*.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1937. Mar. 4. Vol. 30. No. 5. pp. 507–514. [14 refs.]

The authors succeeded in keeping three strains of yellow fever virus in mouse carcinoma 63 for periods varying from 6 to15 months. Young

actively growing tumours were inoculated directly with 0·1cc. of a 10 per cent. suspension of the virus-containing material in serum saline. After 5 to 6 days the tumours were removed from the mice, a portion containing growing cells weighed, then ground up to form a 10 per cent. suspension as before and reinoculated into other actively growing tumours.

With a neurotropic strain after 400 passages in mouse brains, fifty passages in tumours were effected, without any alteration in character being observed. The virus in the primary inoculum was virulent in a dilution of 10^{-8} as compared with 10^{-10} in the 50th passage, therefore, the virus seems to have undergone active multiplication whilst in tumour tissue.

With pantropic tissue-culture virus, 60 passages were made in tumours and material from each passage tested by intracerebral inoculation into mice. No shortening of the incubation period was noticed. There was, however, a slight attenuation of virulence for the hedgehog as tested by the subcutaneous inoculation of 9 animals.

The ordinary pantropic, or viscerotropic virus, was found to show a gradual loss in pathogenicity as tested by inoculations into various animals. In mice inoculated intracerebrally there was a gradual reduction in the incubation period until about the 40th tumour passage when it became stabilized at 7 to 8 days. After 10, 20, 40 and 60 passages respectively, rhesus monkeys and hedgehogs were inoculated subcutaneously with infected tumour material and showed a profound loss of pathogenicity, all 6 monkeys after the 40th and 69th passages surviving without showing any fever, yet developing immunity and the last 4 hedgehogs all surviving. This diminution in pathogenicity was not accompanied by any increase in neurotropism as shown by the results of mouse inoculations.

Yellow fever virus seems to have a special affinity for neoplastic cells, since localization in the cells of the mouse tumour occurs after subcutaneous or intraperitoneal inoculation of the virus. *E. H.*

Hoffmann (W. H.). Die Bedeutung der anatomischen Gelbfieberdiagnose. [**The Importance of the Anatomical Diagnosis of Yellow Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Feb. Vol. 41. No. 2. pp. 195–204.

An article calling attention to the importance of the histological examination of all patients dying after a sudden attack of fever of short duration. Also in view of the fact that approximately 8,000,000 square miles in Africa and South America show serological evidence of the disease, it is evident that in any outbreak histological diagnosis of the infection is of the highest value. *E. H.*

Lynch (Clara J.) & Hughes (Thomas P.) **The Inheritance of Susceptibility to Yellow Fever Encephalitis in Mice.**—*Genetics.* 1936. Mar. Vol. 21. No. 2. pp. 104–112.

Mice from two sources gave different mortality rates when inoculated with the virus of yellow fever, a difference which was maintained in three separate tests. When the strains were crossed the hybrids showed a mortality less than that of the susceptible strain. In one

test the difference was clearly significant and in another it was probably significant. By crossing the hybrid back to the susceptible strain the mortality rate was increased, but by crossing back to a more resistant strain the rate was lowered. This relationship was demonstrated in two tests. When the mice were classified according to parentage, offspring from two susceptible parents were more susceptible than were offspring with one or two resistant parents. Susceptibility did not appear to be modified by sex. Although hereditary factors for resistance to yellow fever encephalitis are present in mice the mode of inheritance is not clear for neither fluctuating variations nor the joint occurrence of a number of genes can be ruled out by the data presented. *G. M. Findlay.*

Stage (H. H.) & Yates (W. W.). **Some Observations on the Amount of Blood engorged by Mosquitoes.**—*Jl. Parasitology.* 1936. June. Vol. 22. No. 3. pp. 298–300.

In the course of certain field work near Portland, Oregon, an unusual opportunity occurred for estimating the amount of blood engorged by *Aedes vexans* and *Aedes aldrichi*, enormous numbers of which fed upon a horse. Groups of unfed and of fully engorged females were weighed, on an analytical balance, within a few hours of capture. Each engorged *Aedes vexans* contained 0·002077±·00012 gram of blood, and each engorged *Aedes aldrichi* contained 0·002107±·000124 gram.

Norman White.

Manteufel (P.). Neuere Untersuchungen ueber das vermeintliche Gelbfieberbakterium *B. hepatodystrophicans* von Kuczynski. [**Later Studies on the Supposed Yellow Fever Bacterium, *B. hepatodystrophicans* of Kuczynski.**]—*Zent. f. Bakt.* I. Abt. Orig. 1937. Feb. 16. Vol. 138. No. 5/6. pp. 306–309.

The author, with Herzberg, previously stated that this organism was identical with *B. renale* (see this *Bulletin*, 1931, Vol. 28, p. 729). As a result of further investigations this organism has been found in the livers and kidneys of cattle, sheep and pigs, as well as rabbits. In addition to yellow fever, joint rheumatism and other diseases have been supposed to be due to its agency. It would seem to be a very wide-spread organism in the blood circulation of man and animals, and is probably identical with *B. lymphophilum* Torrey 1916, and with *Coccobacillus diphtheroides* Collis. It is most closely related to *B. bifidum* of Tissier and probably has a similar physiological significance. *E. H.*

Seiffert (Gustav). Zur Epidemiologie des Gelbfiebers. (Neue Forschungen und praktische Ergebnisse.) [**The Epidemiology of Yellow Fever. New Investigations and Practical Results.**]—*Muench. Med. Woch.* 1937. Feb. 19. Vol. 84. No. 8. pp. 298–301.

A general summary of recent information on the subject containing nothing new. *E. H.*

Findlay (G. M.). Die Immunisierung gegen das Gelbfieber. [**Immunization against Yellow Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Feb. Vol. 41. No. 2. pp. 185–188.

A general summary of various methods used in immunization against yellow fever, together with notes on the different types of virus. *E. H.*

Haagen (E.). Das Gelbfieber. [**Yellow Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Feb. Vol. 41. No. 2. pp. 188–193.

A general account of certain properties of yellow fever virus containing nothing new. *E. H.*

Bablet (J.). La prémunition de la fièvre jaune : réalisations et promesses ? [**Premunition against Yellow Fever. Realizations and Promises ?**]—*Rev. d'Hyg. et de Méd. Préventive.* 1937. May. Vol. 59. No. 5. pp. 321–338. [72 refs.]

A general review of the subject. *E. H.*

Bablet (J.). L'étiologie et l'épidémiologie de la fièvre jaune : conception anciennes. Acquisitions récentes.—*Rev. d'Hyg. et de Méd. Préventive.* 1937. June. Vol. 59. No. 6. pp. 443–465. [52 refs.]

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Adler (S.), Theodor (O.) & Schieber (H.). **Observations on Tick-transmitted Human Spirochaetosis in Palestine.**—*Ann. Trop. Med. & Parasit.* 1937. Apr. 8. Vol. 31. No. 1. pp. 25–35.

The authors have previously recorded the existence of tick-transmitted relapsing fever in Palestine (see this *Bulletin*, 1936, Vol. 33, p. 693) and in the present paper give details of their observations.

Records of 45 cases of the fever, associated with caves, have been collected since 1927; 19 came under their personal observation and the others are from hospital records in Emek Jezreel. Thirteen cases were traced to a single cave near Caesarea; 17 from the neighbourhood of Nazareth; 3 from the foot of Mount Carmel; 1 from upper Galilee and 2 from lower Galilee, so the infection is evidently widely distributed.

In one outbreak, 11 children traced a porcupine to a cave near Kfar Vitkin and whilst 2 watched outside the other 9 entered the cave and remained there two hours. All these 9 children became infected, as did 2 other men who visited the cave later and were bitten by large numbers of the larvae of *Ornithodorus papillipes*.

The incubation period varies from 5 to 9 days, 7 or 8 being the commonest. As a general rule there are one, two, or three attacks, but cases occurred with as many as 14 attacks and all intermediate numbers. The duration of the attacks varies from 3 hours to 4 days, although one case lasted for 19 days; the temperature curves were not typical.

In every attack spirochaetes were present in the blood and the temperature rose to 37·8° to 40°C. Some attacks were accompanied by nausea, vomiting, headache, and pain in the eyes and joints. Neuritis of the sciatic nerve was noted in one case and ocular changes in two. The disease was unaffected by doses of 0·3 to 0·75 gm. neosalvarsan and *Spirochaeta sogdianum*, the causative agent, would seem to be naturally arsenic-resistant.

Ornithodorus papillipes was found to be the transmitting agent both by field observations and also in laboratory transmission experiments. The tick does not pass coxal fluid whilst feeding and therefore this fluid, although infective, is not responsible for producing infection.

All stages of the tick, including the larvae, were found to transmit the infection by bite, and spirochaetes were found in puncture wounds made by infected ticks in man and a rat, 39 and 67 days after the infecting feed. The spirochaetes pass from infected female ticks to the eggs, but not all larvae are infective. *E. Hindle.*

Morrison (R. J. G.). **Some Cases of Relapsing Fever in Palestine.**—*Jl. Roy. Army Med. Corps.* 1937. Feb. Vol. 68. No. 2. pp. 86–94. With 2 figs. & 4 charts.

An account of 4 cases of relapsing fever admitted to the Reception Station, Jerusalem. All the patients were soldiers belonging to the same battalion who had spent a night in an open cave or dug-out and became ill on the 6th or 7th day afterwards. Spirochaetes were

found in the blood of 3 of the patients and although they could not remember having been bitten by lice or ticks, the history of the cases and the results of animal experiments indicate that the infection was probably tick fever, caused by *S. sogdianum*. Guineapigs were susceptible to the infection and also pigs, white mice and rabbits.

Details are given of the clinical history of these cases and attention called to the resemblance to sand-fly fever. However, if the patient is under observation the relapsing nature of the fever is characteristic. Spirochaetes were often difficult to find, even when the temperature was high, but seem most likely to be found during the first febrile attack. *E. H.*

Beck (M. Dorothy). **California Field and Laboratory Studies on Relapsing Fever.**—*Jl. Infect. Dis.* 1937. Jan.–Feb. Vol. 60. No. 1. pp. 64–80. With 1 fig. & 3 charts. [23 refs.]

A general account of field and laboratory studies on relapsing fever in California conducted over a period of three years. The disease is shown to be endemic, 106 cases having been reported from 1921 to 1935. Nine foci of infection have been found in mountainous districts over 5,000 feet high, the most important ones being Big Bear Lake, Lake Tahoe and Packer Lake.

Thirteen strains of spirochaetes resembling *S. recurrentis* have been isolated from chipmunks and Tamarack squirrels (Sierra chickaree) in the field, by subinoculations into mice. In addition six human strains were isolated. Rabbits were found to be more or less refractory to infection although some individuals showed spirochaetes for single days. In guineapigs considerable variation was met with in different strains ; one human strain produced a non-apparent infection, with the blood infective to mice on the 9th, 23rd and 43rd days. Another human strain failed to infect, whilst two chipmunk strains both produced infections with spirochaetes present in the blood for periods up to 8 and 19 days respectively. Brain infections were found to persist in mice up to 114 days after the original infection.

The spirochaetes were found to show remarkable resistance to freezing and even in the tissues of dead animals and in clotted blood would persist for some days. In defibrinated sheep's blood kept in ice they remained viable for at least 195 days.

Hyperimmune guineapig serum was produced against both chipmunk and Tamarack squirrel strains of spirochaetes. Protection was obtained with homologous and heterologous strains and in one instance protection was shown with antiserum produced from a rodent strain against inoculation with a human strain.

The rodent and human strains were found to be identical in morphology and produced similar effects in laboratory animals, and in view of the direct transmissibility of the rodent strains to man there can be no doubt of their identity. *E. H.*

Bruns (A.). Ueber Rückfallfieber in Abessinien. [**On Relapsing Fever in Abyssinia.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Mar. Vol. 41. No. 3. pp. 343–348.

A general account of the disease based on a study of 351 cases in various parts of Abyssinia.

Relapsing fever is endemic in many districts and in addition epidemics may occur, but are confined to the rainy season. In Addis Ababa most of the cases occur in July, August and September, but odd cases occur throughout the whole year.

The question as to whether lice or ticks are the carriers is a little uncertain. In south-east Abyssinia the infection is transmitted by *Ornithodorus moubata*, but also has been shown capable of transmission by the louse. In Eastern Abyssinia the carrier is *Ornithodorus savignyi*; in British Somaliland, *O. moubata*; and in Italian Somaliland both these species have been incriminated and also the louse.

The very fatal epidemic occurring in Djig-Djiga during 1929, at the height of which the number of deaths reached 40 to 50 daily among a comparatively small force of 600 Abyssinian soldiers and a few thousand inhabitants, is stated by the authors to have been transmitted by lice.

Details are given of the clinical symptoms of the disease, which varies considerably in its mortality, depending mainly on the presence or absence of other infections and the general health of the patient. As a rule the average mortality is about 10 per cent.

Although tick transmitted cases of relapsing fever are not infrequent, the disease seems to be generally transmitted by lice and the usual methods of prophylaxis are effective. *E. H.*

Sibilia (Daniele). Primo contributo alla conoscenza della spirochaeta recurrentis osservata in Addis Abeba. [**Relapsing Fever in Addis Ababa.**]—*Policlinico.* Sez. Prat. 1937. Apr. 19. Vol. 44. No. 16. pp. 772–776. [20 refs.]

The author has had under his observation forty cases of relapsing fever during the early months of the Italian occupation of Addis Ababa. The spirochaetes seen in smears were, he thought, of the Obermeier type, varying in length from 10–45 μ, but more slender than usual, 0·25 μ mostly. Many were quite short, 4–10 μ only. The vector was the louse. He remarks that louse-borne relapsing fever has not previously been recorded in the territory, the usual being the tick-borne *duttoni* type. *H. H. S.*

Clark (E. M.). **Report on Relapsing Fever in Burao.**—*Somaliland Protectorate Ann. Med. & San. Rep. for Year ending 31st December, 1936.* Appendix II. pp. 57–66. With 2 graphs.

An interesting account of relapsing fever in Burao, Somaliland, where the disease in recent years has become a serious problem.

It is supposed to have spread from Abyssinia, and was first noted in Burao in 1927. The number of cases rose from 13 in 1929, up to 100 or more in 1932, 500 in 1933, and 618 cases in 1936. The number of cases begins to rise each year from April to September, after which there is a rapid fall. The population is lowest during these months and there is no obvious explanation of this seasonal prevalence of the disease.

The disease is of a mild type, and out of 981 treated cases there have been only 6 deaths; but untreated cases have a higher mortality and it is estimated that annually about 50 to 100 people die of relapsing fever out of a population of approximately 15,000.

The vector seems to be mainly *Ornithodorus savignyi*, which has a very localized distribution, but is to be found under many of the trees, especially where stock is tied, as well as in the houses and Haafa town. The disease started in the largest mosque in the town, and as this was used as sleeping quarters for a changing population, it must have acted as a focus for the spread of infection. The ticks inhabit loose sand and not matting, so by moving the sites of infected camps it should be possible to reduce the incidence of the disease.

In a note signed by Dr. J. C. R. Buchanan, it is pointed out that Drake-Brockman, the first to report Relapsing Fever in British Somaliland [see this *Bulletin*, 1914, Vol. 3, p. 4] predicted a spread to Berbera, but fortunately this did not prove a true prophecy, and now the disease seems to have disappeared from the coast. *E. H.*

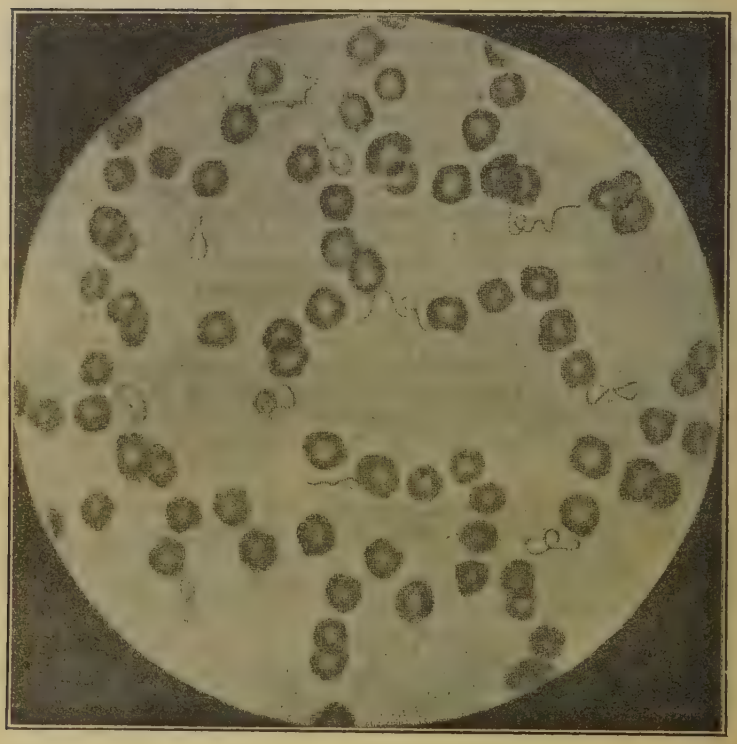
Modugno (Gastone). La febbre ricorrente in Somalia. Osservazioni cliniche ed epidemiologiche. [**Relapsing Fever in Somalia. Clinical and Epidemiological Observations.**]—*Giorn. Ital. di Clin. Trop.* 1937. Feb. 28. Vol. 1. N.S. No. 2. pp. 35–6, 39–42. With 6 charts.

Between 28th July and 10th November, 1935, there were 142 cases of relapsing fever in Somalia coming under the author's notice; 92 were proved by blood examinations. Most of the cases were fairly typical but in some the symptoms were strongly indicative of bilious remittent malaria. Twenty showed severe symptoms during the apyrexial period, and two had a marked meningeal reaction—rigidity of the neck, Kernig's sign positive—but the prognosis was favourable; most of the cases were mild and there were only three deaths. *Ornithodorus moubata* was not found, but lice were common.

H. H. S.

Taddia (Leo). Febbre esantematica da spirochete in Somalia. [**Spirochaetal Fever in Somalia.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1937. Feb. Vol. 18. No. 2. pp. 106–110. With 1 chart & 1 fig.

The patient, a soldier of unknown age, complained of headache, weakness, loss of appetite, photophobia and lumbar pain. His temperature ranged between 39° and 40·4°C. for 5 days, spleen a little enlarged, albuminuria present and a polymorphic rash over face, chest and arms. The temperature then came down by crisis and for 7 days there was no fever, but a feeling of debility, and desquamation occurred on the site of the rash. Then the temperature rose rapidly to 40·2°, falling again to normal, the fall being accompanied by a profuse sweating; the following day this rise and fall were repeated. During the febrile period examination of the blood revealed filiform bodies 8–24μ or even to 30μ in length and 0·3μ broad, as many as 5 or 6 in a field. What these are is not known. The fever is not like ordinary relapsing fever and the filiform bodies are not like *Sp. obermeieri* [the illustration shows them to resemble very minute filarial embryos, in the disposition of their curves]. There was during the fever "intense leucocytosis with polynucleosis" [but no figures are given]. *H. H. S.*



Microphotograph of blood showing filiform bodies from patient diagnosed as suffering from spirochaetal fever in Italian Somalia. [TADDIA's paper.]

[Reproduced from the *Archivio Italiano di Scienze Mediche Coloniali e di Parassitologia.*]

RAMIJEAN (R.), HUONG (N. V.) & FARINAUD (M.). Deux cas de fièvre récurrente dans la région Saïgon-Cholon. [**Two Cases of Relapsing Fever in the Saïgon-Cholon Region.**]—*Bull. Soc. Path. Exot.* 1937. Mar. 10. Vol. 30. No. 3. pp. 220–224.

For many years an average of 50,000 blood films have been examined in this region without finding any trace of spirochaetes and therefore the sudden occurrence of two cases of relapsing fever among Chinese immigrants presents some interest from an epidemiological point of view.

After considering the evidence the authors are of the opinion that both cases acquired the infection from infected lice either derived from an undetected carrier who had passed through the Immigration, or, in view of the incubation period in lice, the patients may have carried lice with them from China, and these insects produced the infection after their arrival in Saigon. *E. H.*

RAMIJEAN (R.), FARINAUD (M. E.) & TRAN-VAN-TAM. Deux cas de fièvre récurrente dans la région Saigon-Cholon. [**Two Cases of Relapsing Fever in the Saigon-Cholon District.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1937. Feb. Vol. 15. No. 2. pp. 133–140. With 2 charts.

A more detailed account of the cases previously recorded [see above].

E. H.

CUNNINGHAM (J.) & FRASER (A. G. L.). **Further Observations on Indian Relapsing Fever. Part III. Persistence of Spirochaetes in the Blood and Organs of Infected Animals. Part IV. Re-Infections and Super-Infections.**—*Indian Jl. Med. Res.* 1937. Jan. Vol. 24. No. 3. pp. 571–580. [61 refs.]; 581–592. [15 refs.]

i. Using squirrels infected with *S. carteri*, the authors have attempted to prove, by means of subinoculations, the presence or absence of spirochaetes in the tissue after varying periods, and also to determine the type of spirochaete recovered. The results indicate that residual infections, and particularly invasion of brain tissue, do not occur with the Indian louse-borne strain. The infected animals maintain spirochaetes in the blood and internal organs throughout the interval between the first and second attacks, and the spirochaete recovered during the interval always differs in type from that of the primary attack. The serological examination of the blood, carried out at various periods during and subsequent to infection, bears out the conclusion that the disease in most cases consists essentially of a succession of invasions by different types of spirochaetes which vary in intensity and duration, the essential difference between cases showing single attacks from those with relapses, being only one of degree, in that later attacks are latent in one case and demonstrable by blood examination in the other.

ii. The agglutinin content of the serum of five monkeys infected with different serological types of *S. carteri* was tested at 30-day intervals, and antibodies found in the blood for periods up to 19 months after the primary infection. With the disappearance of antibody the animals become completely susceptible to re-infection. When antibody is present the success or failure of re-infection depends upon the size of the dose, the type of spirochaete, and the concentration and types of antibody produced by the primary infection. Under ordinary conditions re-infection will fail when sufficient antibody to the type of spirochaete used for re-infection is present in the blood, but when the antibody is absent or insufficient, re-infection can readily be obtained. A rapid and considerable increase in the corresponding antibody content of the blood is produced by re-infection with either homologous or heterologous types.

Superinfections follow the same general rules and whilst antibodies from the primary infection are present in the blood, superinfections are only successful with heterologous types. During its course such an infection can be distinguished from the different stages of the primary infection by serological tests, even when it has been

superimposed during the first attack. The clinical appearances depend upon the particular stage of the disease chosen for superinfection.

E. H.

ADLER (S.) & ASHBEL (Riwkah). **Observations on *Spirochaeta sogdianum* Nicolle and Anderson, 1928, in Laboratory Animals.**—*Ann. Trop. Med. & Parasit.* 1937. Apr. 8. Vol. 31. No. 1. pp. 89–104. With 9 figs. on 2 plates.

A detailed study of 6 strains of *Spirochaeta sogdianum*, one obtained by feeding wild ticks, *O. papillipes*, on a guineapig, and the other 5 from 4 human cases. Two strains were obtained from the same case (4th and 10th relapses).

The spirochaete was found to be infective for mice, rats, field-mice (*Microtus guentheri*), guineapigs, rabbits and dogs. In splenectomized rats and field-mice the infection was heavier and more prolonged than in normal animals. The fluid from the anterior chamber of the eye was found to be infected, and also the spirochaetes can pass through the placenta of the guineapig and infect the offspring. Guineapigs were found to be the most suitable host and out of 290 individuals only two were refractory. The spirochaete is strongly neurotropic and in guineapigs that have passed through even a slight infection the spirochaete persists in the brain up to at least 130 days after recovery. Guineapigs that have passed through a moderate or severe infection are immune to reinfection with the same strain, but can be reinfected by any other strain. Even the two strains isolated from the same human case (4th and 10th relapse) could be distinguished by their cross-immunity and agglutination tests.

Convalescent sera, in addition to agglutinating and immobilizing homologous spirochaetes, contain a specific factor which causes these organisms to attach themselves to lymphocytes, mononuclears and polymorphs, and to the nuclei of these cells after disintegration of their protoplasm. This factor causes the entrance of spirochaetes into polymorphs in the complete absence of phagocytic activity. Convalescent sera have no curative or prophylactic value. *E. H.*

FENG (Lan-Chou) & CHUNG (Huei-Lan). **Attempts to infect *Ornithodorus moubata* with the Chinese Strain of *Spirochaeta recurrentis*.**—*Proc. Soc. Experim. Biol. & Med.* 1937. Apr. Vol. 36. No. 3. pp. 330–333.

Four lots of young larval *Ornithodorus moubata* and adult male and female specimens, were fed on squirrels heavily infected with the Chinese strain of *Spirochaeta recurrentis* and subsequently fed on normal squirrels and also examined for spirochaetes.

The feeding experiments were uniformly negative and at 25–28°C. the spirochaetes both in the guts of the ticks and also in the coelomic fluid degenerated and finally disappeared about 6 days after the infecting feed. The injection of emulsions from these ticks also failed to infect squirrels.

These findings suggest that the Chinese strain of relapsing fever is biologically different from those transmitted by ticks and also from the Russian and American strains, which seem to be transmissible by *O. moubata*. *E. H.*

HORRENBERGER (R.). Les rats d'Alger réservoir de virus de la fièvre récurrente hispano-africaine. [**Rats as a Reservoir of Spanish-African Relapsing Fever in Algiers.**]—*Arch. Inst. Pasteur d'Algérie.* 1936. Dec. Vol. 14. No. 4. pp. 421–423.

The author gives the results of an examination of 23 lots of 10 rats each, caught in Algiers during 1933 and 1934. Among these 23 lots, three were found to be infected with *S. hispanicum* as determined by inoculation of brain emulsions of the rats into guineapigs. It is assumed that probably only one rat in each of these three lots was infected, giving an infection rate approximately the same as that found by SERGENT—one out of 90. *E. H.*

LEPTOSPIROSIS.

LUMLEY (George F.). **Leptospirosis in Queensland: a Serological Investigation leading to the Discovery of Distinct Serological Groups of Leptospirae causing Leptospirosis as it occurs in Northern Queensland, with Some Other Related Observations.**—*Med. Jl. Australia.* 1937. May 1. 24th Year. Vol. 1. No. 18. pp. 654–664. [40 refs.]

A detailed study of strains of leptospira isolated from man and rat in the Ingham-Inisfail area of northern Queensland.

The results show the existence of two separate and distinct serological groups, tentatively named Group Australis A and Group Australis B.

Cross-agglutination tests with the sera of 24 patients showed that 10 belonged to group A and 14 to group B. Each group contains both human and rat strains, and it would appear that the passage of rat strain through man does not materially alter its agglutination properties. These two strains are not related to the Pomona strain [see below] nor to Strain R. 102 from southern Queensland. Neither are they related to any of nine water strains isolated from Ingham water. Australis A is not related to any of the over-sea strains examined, but Australis B was found to be distantly related to *L. icterohaemorrhagiae* (Wijnbergi, Netherlands) and to *L. canicola* (Wubbeling). Both A and B cultures have been kept in cultures more than 18 months without showing any alteration in their agglutination characteristics, the preservation of which does not seem to require frequent passaging through guineapigs to maintain virulence.

Stocks of leptospiral antiserum prepared in England against ordinary infections, did not agglutinate Australis A and had little effect on Australis B and it is evident that an active antiserum for local use would have to be made from these two strains. Attention is called to the allergic reactions that may occur after the administration of anti-leptospiral serum.

In addition to the existence of these two well marked types of infection, there is a suggestion that sub-types of *Leptospira icterohaemorrhagiae* and perhaps *L. canicola* may be present.

E. Hindle.

Clayton (G. E. B.) & Derrick (E. H.). **The Presence of Leptospirosis of a Mild Type (Seven-Day Fever) in Queensland. With a Foreword by** Raphael Cilento.—*Med. Jl. Australia.* 1937. May 1. 24th Year. Vol. 1. No. 18. pp. 647–654. With 5 charts.

The description of a case of seven-day fever occurring in a patient living near Pomona, South Queensland. This is the first record of the existence in Australia of mild strains of leptospirosis similar to those existing in other countries. The authors diagnosed the case clinically, from the similarity of the symptoms to those of the seven-day fever of the East, and succeeded in isolating a leptospira from the patient's blood which in guineapigs showed a much lower virulence than the ordinary strain of *L. icterohaemorrhagiae.* Thus 20 out of 22 animals inoculated with the Pomona strain survived, whilst 10 out of 11 died when infected with the ordinary Weil strain in Queensland.

Details are given of the infection in guineapigs, and it is shown that the carrier condition may develop in these animals, one guineapig showing leptospira in its urine 114 days after inoculation. Two wild rats were inoculated but showed no obvious signs of infection; yet when respectively 8 and 20 days after inoculation the liver and kidney of these animals were injected into guineapigs, these became infected.

Cross-agglutination tests showed that the Pomona type is distinct from the ordinary Weil's disease strain, but some slight degree of cross protection was obtained with the Ballico strain. Comparison with foreign strains showed that it is related to the Rachmat and Baermann strains from Sumatra.

The authors produce clinical evidence in support of the view that an endemic centre of this disease occurs in Queensland, about 700 miles further south than the area affected by the more severe type of leptospirosis. *E. H.*

Schüffner (W. A. P.) & Walch-Sorgdrager (B.). Infection humaine par *Leptospira canicola.* [**Human Infection with** *L. canicola.*]—*Bull. Office Internat. d'Hyg. Publique.* 1937. Feb. Vol. 29. No. 2. pp. 297–306. With 2 charts.

A description of two new cases of human infection with the dog strain of leptospira, *L. canicola,* observed during 1936.

The serum reaction of the first case gave agglutinations of 1 : 100 against *L. icterohaemorrhagiae* as compared with 1 : 3,000 against *L. canicola*; the urine remained negative. In the second case the titre rose to 1 : 10,000 against *L. canicola* and was only 1 : 300 against *L. icterohaemorrhagiae.* A strain of *L. canicola* was obtained by inoculation of the urine into a guineapig, which showed a very benign infection. In this case the source of infection was probably a dog owned by the patient's family, which showed an agglutination of 1 : 30,000 against *L. canicola* and only a doubtful reaction in 1 : 10 dilution against the ordinary strain.

The authors give a brief summary of the three European leptospiroses which are well defined by their clinical, bacteriological and epidemiological characters. The first of these is the ordinary Weil's disease caused by *L. icterohaemorrhagiae,* and is spread throughout the world; the second type caused by *L. canicola,* a dog strain, up to

now has been found only in Holland ; the third is the so-called " Slime Fever," which causes symptoms resembling an intestinal form of influenza. *E. H.*

Chodzko (W.). Spirochétose ictéro-hémorragique en Pologne. [**Spirochaetal Jaundice in Poland.**]—*Bull. Office Internat. d'Hyg. Publique.* 1937. Feb. Vol. 29. No. 2. pp. 307–316. [25 refs.]

A general summary of observations on Weil's disease in Poland, in which it is mentioned that 15 cases have been recorded there, of which one was a laboratory infection, with 5 deaths. The patients were all males who became infected during the summer, and in 9 of them the symptoms developed soon after bathing in the open air. Although up to the present, no epidemics have been noted, in view of its economic importance and the efficiency of methods of protection, the author considers that all cases of infection and deaths should be notified to the public authorities. *E. H.*

Rimbaud (L.), Janbon (M.) & Labraque-Bordenave. Trois cas de spirochétose ictéro-hémorragique chez des mineurs. [**Three Cases of Weil's Disease in Miners.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1937. May 17. 53rd Year. 3rd Ser. No. 16. pp. 604–610.

A description of three typical cases of Weil's Disease occurring in coal miners at Rochebelle, Alès (Gard). Attention is called to the importance of the manner in which the urea is eliminated by the urine. In these cases the azoturic crisis commenced respectively on the 15th, 16th and 11th days of the disease, and very soon reached its maximum, in two cases the amount of urea reaching 68 gm. per 24 hours. The authors are of the opinion that the hyperazotaemia occurring in this disease is for the most part extra-renal.

E. H.

Rimbaud (L.), Janbon (M.) & Labraque-Bordenave. Deux cas atypiques de spirochétose ictéro-hémorragique. Formes anictériques [pseudo-grippale et méningo-rénale]. [**Two Atypical Cases of Weil's Disease. Forms without Jaundice Pseudo-Influenzal and Meningo-Renal.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1937. May 17. 53rd Year. 3rd Ser. No. 16. pp. 610–615.

A description of the clinical symptoms of two atypical cases of Weil's disease occurring in Montpellier, where the disease is rare. Neither case showed signs of jaundice, or haemorrhages, and the method of infection remained obscure. The first closely resembled a case of influenza, but its nature was determined by the systematic examination of the urine which showed a polyuric crisis, and by sero-diagnostic tests.

The second case showed a febrile syndrome with vomiting, then a morbilliform erythema, and a secondary meningitic syndrome with hyper-leucocytosis (216 elements) of the cerebrospinal fluid. It gave a strongly positive sero-diagnostic reaction against *S. icterohaemorrhagiae.* *E. H.*

Bewley (G.) & Wilson (J. G.). **A Case of Weil's Disease.**—*Irish Jl. Med. Sci.* 1937. Mar. 6th Ser. No. 135. pp. 123–125.

A clinical description of a case of Weil's disease which developed 14 days after the patient had been bitten by a rat. Although the inoculation of urine into a guineapig was negative, the patient's serum agglutinated a formalinized culture of *Spirochaeta icterohaemorrhagiae* in all dilutions from 1/10 to 1/30,000. A second case of this disease is recorded from Ireland in which the patient, who had a cut foot, bathed in a pool in a rat-infested area in Baldonnel. *E. H.*

Vaucel (M.) & Soulier (R.). Sur l'existence d'un foyer de leptospirose à Tuyen-Quang (Tonkin). [**On the Existence of a Centre of Leptospirosis at Tuyên-Quang (Tonking).**]—*Bull. Soc. Path. Exot.* 1937. May 12. Vol. 30. No. 5. pp. 408–416.

A study of a centre of leptospirosis in the middle region of Tonking, discovered by means of sero-diagnostic tests, and its nature confirmed by the isolation of a leptospira morphologically identical with *S. icterohaemorrhagiae.*

Serum reactions, in which 10 strains of leptospira were used, gave 54 positive results out of 195 patients. Of these *S. icterohaemorrhagiae* was agglutinated preferentially 42 times; *S. autumnalis* 4 times; *S. Kebler* (*autumnalis* ?) twice; whilst *S. hebdomadis* and *S. Tuyên-Quang* were never agglutinated preferentially. In six cases the agglutination was equal for two different species.

The organism isolated was pathogenic for guineapigs, and agglutination and other tests indicate that it was related to both *S. Tuyên-Quang* and *S. icterohaemorrhagiae.*

Only 10 per cent. of the patients showed typical clinical signs of the infection, and the great majority arrived at the hospital for malaria or other ailments.

In cases of simple leptospirosis the proportion of positive serum diagnoses did not exceed 60 per cent. and in other patients showing less well marked symptoms the positives were only about 25 per cent. The extreme specificity of the antigens, and the persistence of agglutinins, together limited the value of sero-diagnostic tests for the infection.

There was no correlation between any strain of leptospira and any particular clinical type. *E. H.*

Vaucel (M.). Leptospiroses anictériques au Tonkin. [**Leptospiroses without Jaundice in Tonking.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1936. Oct. Vol. 14. No. 8. pp. 1115–1131. With 10 charts.

The author has collected observations on 10 cases of leptospiral infection in which jaundice was absent. In 9 cases, agglutination and inoculation tests showed that the infection was *L. icterohaemorrhagiae*, whilst in one case the spirochaete was very distinct, but is classified under the *L. autumnalis* group.

Although these cases clinically resembled similar cases in Japan, the Dutch East Indies and also in France, it was found very difficult to establish any precise diagnosis by means of agglutination tests and it is evident that in Tonking there are antigenic differences between the

various strains of *L. icterohaemorrhagiae*. It is certainly the same for *L. autumnalis* and *L. hebdomadis* and the author insists on the necessity of using several strains including locally isolated ones, in making agglutination tests. *E. H.*

VAUCEL (M.). Séro-diagnostic des leptospiroses au Tonkin agglutinines et co-agglutinines. [**The Sero-Diagnosis of Leptospiroses in Tonking. Agglutinins and Co-Agglutinins.**]—*Bull. Soc. Path. Exot.* 1937. Feb. 10. Vol. 30. No. 2. pp. 176–186. [15 refs.]

The author has made 643 sero-diagnostic tests during 1936 on patients in Tonking, with the following results :—

(1) 21·8 per cent. positive in 329 patients suspected of leptospirosis.
(2) 4·05 per cent. positive in 164 patients with indeterminate fever.
(3) 11·8 per cent. positive in 137 patients whose serum had been forwarded for Wassermann tests.
(4) 15·3 per cent. positive in 13 patients infected with pyomyositis.

Four strains of *L. icterohaemorrhagiae* isolated from rats in Hanoi, as well as Japanese strains of this species and of *L. autumnalis* and *L. hebdomadis*, were used for their reactions.

With reference to *L. icterohaemorrhagiae*, 36 per cent. of the cases agglutinated all the strains, 33 per cent. showed very different degrees of activity against the various strains, and 10 per cent. of the cases reacted only with one particular strain.

Out of 92 positive sera, 48 agglutinated *L. autumnalis*, and 4 of these were negative with all other strains, 5 sera agglutinated *L. autumnalis* at higher dilutions than *L. icterohaemorrhagiae*, 3 sera agglutinated the two at equal dilutions, and in 36 sera the titre of *L. autumnalis* did not exceed 1 : 100 as compared with much higher titres in the case of strains of *L. icterohaemorrhagiae*. Up to the present no serum has been found which agglutinated *L. hebdomadis* exclusively, or in a higher titre than that of the strain with which it was associated.

A zone phenomenon was observed in 77 per cent. of the positive sera in titres below 1: 1,000, but was present in only 2 per cent. of the sera with titres of 1: 1,000 or higher.

The serum of guineapigs surviving a single inoculation of the products of leptospiral cultures, develop agglutinins and facilitate the biological diagnosis of leptospirosis. *E. H.*

T'ANG TZE-KUANG. **The Occurrence of Weil's Disease in Canton, China.**—*Chinese Med. Jl.* 1937. Apr. Vol. 51. No. 4. pp. 483–488. With 1 plate.

A description of three typical and fatal cases of Weil's disease in Canton, the first record of its occurrence in China.

The blood of one patient was inoculated into guineapigs, and reproduced the infection, leptospira being found in sections of the organs. From the data concerning another patient the disease could be traced back to an epidemic in the City Detention Home, resulting in more than 100 deaths within three to four months, and only terminated when the inmates were removed to new quarters. The clinical features of these cases were all typical, with jaundice, late subcutaneous haemorrhages, cerebral symptoms and fulminating course ending in death. *E. H.*

Bigot (A.). Observation clinique d'un cas de spirochétose ictéro-hémorragique. [**Clinical Observations on a Case of Weil's Disease.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1936. Oct. Vol. 14. No. 8. pp. 1132–1136. With 1 chart.

A detailed account of the symptoms of a fatal case of infection with a spirochaete morphologically resembling *L. icterohaemorrhagiae*. The patient showed a descending febrile attack which rose very suddenly before death. Other symptoms were vomiting, muscle pains, and a slight yellowish tinge. There was a marked rise in the urea content of the blood, albuminuria, and increased tension of the cerebrospinal fluid. *E. H.*

Lesné (E.), Troisier (J.) & Bénard (H.). Une spirochétose nouvelle. [**A New Spirochaetosis.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1937. Mar. 22. 53rd Year. 3rd Ser. No. 10. pp. 368–374. With 4 figs.

The patient, a girl 13 years old, entered hospital with diffuse abdominal pains, accompanied by vomiting and constipation. Febrile symptoms continued for about 3 weeks with temperatures oscillating daily between 38° and 39°C., terminating with complete recovery after defervescence with lysis. The symptoms being suggestive of appendicitis, laparotomy was performed, but the removed appendix showed no signs of infection.

The spirochaete obtained by blood culture, when inoculated intravenously into two human subjects and a monkey, after an incubation period of 4 to 8 days produced a marked febrile attack (40°C.) lasting for 1 to 2 days followed by recovery without any relapses. The organism, named *S. haemophilus* [sic], seems to resemble in some respects *Spirochaeta sinensis* found by Pons (see this *Bulletin*, 1924, Vol. 21, p. 471) in the blood of an Annamite in Saïgon. The pathogenic problem of these isolated infections remains very obscure. *E. H.*

Troisier (Jean) with the collaboration of J. Sifferlen. *Spirochaeta haemophilus.*—*Ann. Inst. Pasteur.* 1937. Mar. Vol. 58. No. 3. pp. 233–246. With 6 figs. (4 charts).

The authors, by means of blood culture, isolated a spirochaete, to which they give the name *S. haemophilus*, from the circulation of an infant who showed symptoms suggesting typhoid fever. The organism grows readily at 37°C. in a mixture of 1 part fresh blood in 4 parts of Martin's bouillon, adjusted to pH 7·4; subcultures are made every 10 days. In morphology it is clearly distinguished from leptospira, and although variable its average length is 9μ, with about 5 turns of the spiral.

Cultures were inoculated into various laboratory animals with negative results and only in man and monkeys (*Cercopithecus callitrichus*) was any pathogenic action detected. Generally after an incubation period of 4 to 8 days there was a short rise in temperature not followed by any relapse. Occasionally chronic and inapparent infections were produced which could only be recognized by blood culture.

Agglutination tests with human and monkey convalescent serum gave negative results, but the serum of two fowls inoculated with cultures agglutinated after one month in dilution of 1: 800 and 1: 1,000, falling after 3 months to 1 : 200 and 1 : 300 respectively. However, these birds show no sign of infection when inoculated with cultures of the spirochaete. *E. H.*

DE LAVERGNE (V.) & ACCOYER (H.). La spirochétose méningée pure. Considérations épidémiologiques et pathogéniques. [**Simple Meningeal Spirochaetosis. Epidemiological and Pathogenic Considerations.**]—*Rev. d'Hyg. et de Méd. Preventive.* 1937. May. Vol. 59. No. 5. pp. 339–352. [15 refs.]

A general discussion of the problem with special reference to the increasing frequency of the meningeal form of infection with *S.* (*Leptospira*) *icterohaemorrhagiae.*

In 1935 this disease was made notifiable in France and the authors recommend that all specimens of serum sent to the Pasteur Institute for testing should be accompanied by a description of the clinical symptoms, in order to obtain further information of the various forms of this disease. *E. H.*

ZIMMERMANN (E.) & UFFENORDE (H.). Ueber die Haltbarkeit der Seren gegen Weilsche Krankheit. [**The Durability of Weil's Disease Anti-Sera.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1937. May 27. Vol. 90. No. 4. pp. 319–323.

The authors tested the persistence of the immune bodies in convalescent human sera from cases of Weil's disease, and also samples of rabbit anti-sera.

The results of agglutination and lysis tests show that generally the human anti-sera lose their strength within a comparatively short time, whilst the rabbit anti-sera were still active after more than a year. No appreciable differences were noted in the keeping qualities of sera containing 0·5 per cent. phenol and those without any such preservative. *E. H.*

SANDIFORD (B. R.). **A Note on Leptospira Icterohaemorrhagiae in Egyptian Rats.**—*Jl. Egyptian Med. Assoc.* 1936. Nov. Vol. 19. No. 11. pp. 687–688.

The author examined for leptospira the kidneys of 23 rats, all *Rattus rattus* except two *R. norvegicus*, caught in a village in Behera province, both microscopically and by subinoculation into guineapigs, with negative results. [The absence of leptospiral infection in Egyptian rats is noteworthy in view of its prevalence in many other parts of the world.] *E. H.*

MASON (Neil). **Leptospiral Jaundice occurring naturally in a Guinea-Pig.**—*Lancet.* 1937. Mar. 6. pp. 564–565.

A record of a fatal case of leptospiral jaundice occurring in 1 out of 12 guineapigs which arrived at the Liverpool City Laboratories. The infection was probably derived from rats at the dealers, since 10 days previously rats had broken in and killed 2 or 3 of his guineapigs.

The occurrence of a natural infection of this nature is of interest in view of the general use of these animals for the diagnosis of Weil's disease. *E. H.*

SMITH (J.). **Vaccination of Guinea-Pigs and Human Beings against Leptospiral Infections.**—*Jl. Hygiene.* 1937. Apr. Vol. 37. No. 2. pp. 261–270. [20 refs.]

The author has studied the results of vaccinating guineapigs with various strains of leptospiral infections and human beings with killed suspensions of virulent *L. icterohaemorrhagiae.*

Thirty-six guineapigs were inoculated, each with 2 doses of 1 cc. of a non-virulent culture of *L. icterohaemorrhagiae* and when subsequently inoculated with a virulent strain, all the vaccinated animals survived, whilst all the controls (18) died of leptospirosis. Complete protection was also obtained by the inoculation of cultures killed either by heat or by chemical agents (48 hours exposure to either 0·5 per cent. phenol, 0·5 per cent. formalin, or 0·5 per cent. dettol).

In addition, guineapigs were vaccinated with heterologous strains, including living and killed *L. canicola*, and living strains of *L. icterohaemorrhagiae* (Rachmat), *L. hebdomadis* and *L. biflexa* respectively. Complete protection against virulent *L. icterohaemorrhagiae* was obtained with *L. canicola*, incomplete protection with the Rachmat strain and *L. hebdomadis*, and no protection with the saprophytic strain, *L. biflexa.*

The lytic titres of vaccinated guineapigs varied from 1 : 10 to 1 : 100 in the case of those inoculated with 2 doses of non-virulent *L. icterohaemorrhagiae*, whilst those vaccinated by phenolized cultures were significantly lower, the titres ranging from 1 : 6 to 1 : 10.

The inoculation of virulent cultures following upon vaccination resulted in the development of the carrier condition, with presence of virulent spirochaetes in the kidneys of some of the guineapigs that had been vaccinated with chemically killed leptospira, and also with living non-virulent cultures of the Rachmat strain.

The vaccination of human beings gave somewhat disappointing results. Killed vaccines of both virulent and non-virulent strains were inoculated into a first series of 82 patients, each receiving a first injection of 1 cc. of a killed culture and a week later a second injection of 2 cc. In this series 33 returned for blood examination, and of these 24 gave entirely negative tests ; in 7 the serum reacted to a titre of 1 : 10, and in only one case to 1 : 30. In a second series 40 patients were similarly vaccinated and of the 15 tested only 4 reacted to a titre of 1 : 10 with *L. icterohaemorrhagiae.*

A third series of 28 patients were vaccinated with a commercial leptospiral vaccine used for dogs and foxes, and again only 3 out of 13 tested reacted in a 1 : 10 dilution.

These findings indicate the necessity for increased dosage to stimulate the further production of immune bodies. *E. H.*

MALARIA.

Barber (M. A.) & Rice (J. B.). **A Survey of Malaria in Egypt.**—*Amer. Jl. Trop. Med.* 1937. May. Vol. 17. No. 3. pp. 413–436.

This is a survey of malaria in the Valley of the Nile, including Fayum, the Siwa Oasis in the Western Desert and in the Suez Canal Zone. The observations recorded were made between August and December, 1936. Malaria was found to be widespread in the Nile Valley. Parasite and spleen indexes were high in the vicinity of rice-fields or of large bodies of fresh water; they were commonly low elsewhere. High indexes are reported from the Siwa Oasis and the Suez Canal Zone. *Pl. falciparum* was found in the majority of places surveyed, but *Pl. vivax* predominates. *Pl. malariae* was found in the Siwa Oasis and in the Canal Zone but not in the Nile Valley. The strain or strains of *vivax* met with in Egypt are less apt to cause enlarged spleen and severe illness than the local strains of *falciparum*.

A. pharoensis, *A. multicolor* and *A. mauritianus* are common in the Nile Valley; *A. pharoensis* is an efficient vector of malaria. It has an avidity for human blood. Many specimens were found naturally infected with oöcysts, a few with sporozoites. It can be readily infected in the laboratory with both *falciparum* and *vivax*. It frequents man-inhabitated tents much more frequently than houses or stables. Its distribution in the Delta agrees with the distribution of malaria. *A. multicolor*, which is also very prevalent, can be infected in the laboratory; no naturally infected specimen was taken. *A. sergenti* was found in the Siwa Oasis and in the Canal Zone. No positive evidence of its importance as a vector was forthcoming.

The authors consider that eradication of malaria would not be possible without a radical change of the system of irrigation. The prohibition of rice cultivation in the neighbourhood of large centres of population might be useful. As a palliative the distribution of *Gambusia* is recommended. *Norman White.*

Egypt, Ministry of the Interior. Dept. of Public Health. Eleventh Annual Report on the Anti-Malaria Campaign in Egypt, 1934.—17 pp. With 4 maps and 3 graphs. 1936. Bulâq, Cairo: Govt. Press. [P.T. 7.]

Reed (J. G.). Malaria in Relation to the Composition of Soil and Water. A Paper read at the Half-Yearly General Meeting of the Batang Padang District Planters' Association, held at Sungkai on October 28th, 1936. 7 pp.

Elsbach (E. M.). Orienteerend malaria- en filariaonderzoek in Nieuw-Guinea. [**Preliminary Survey of Malaria and Filariasis in New Guinea.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1937. Apr. 27. Vol. 77. No. 17. pp. 1036–1054. With 1 map & 3 figs. on 1 plate.

There was little time and opportunity for the investigator in this expedition, designed to choose a place of settlement on the lower waters of the River Digoel, to make any far-reaching research into the prevalence of malaria and filariasis among the people of the rivers of South-West New Guinea. It amounts simply to a record of figures for men, women and children at certain seasons of the year.

Interesting details are given of the character of this comparatively little known country, which are worthy of record. The rivers were the Digoel in its upper and lower reaches, its tributaries, the Mappi river and a river, the Kawarga, which joins the Digoel and the Mappi. The tribes inhabiting this region take their names from the river on which they live. They are not, however, really resident, but in a state of constant journeying from one forest clearing to another and they are also in a state of constant warfare with one another. One race is dominant among them, of fine physique and greatly feared by the rest. This race inhabits the shores of the Mappi river. They form a marked contrast to the inhabitants on the Digoel river, who are wanting in bone and muscle, have enlarged spleens and marked lumbar lordosis. Some of these differences, and also some of the lessened resistance to disease, shown by the various tribes may be related to their dietary level. Thus a marked difference exists in the type of soil of the upper Digoel and the lower Digoel. In the case of the former the soil has only a thin covering of humus, which is liable to be washed away by the heavy rain as soon as the forest has been cleared. In the case of the latter a layer of humus 30 cm. thick is present, which ensures the growth of abundance of green vegetables and even tomatoes. The Mappi Papuans, whose robust physique was specially notable, obtain abundance of fresh meat, fowls and fish. A small point illustrates very well the different outlook of this race from that of the others. The Mappians, in their bartering, do not choose such decorative articles as beads and mirrors, but prefer fish-hooks and matches.

So far as the actual field investigation went, it was found that the malaria parasitic indices at Koholombo and Wap, representing Mappians, were 6·3 and 8·4 per cent., whereas at Imahoi, a lower Digoel locality, it was 10·5. The filaria investigation at Koholombo and Wap, relating to *F. bancrofti*, gave indices of 12·9 and 9·3 per cent. In this region the vector mosquitoes are the same for both malaria and filariasis and belong to the Australasian fauna. The vector mosquitoes, which are anthropophilic, are *A. punctulatus typicus*, its variety *A. punctulatus moluccensis* and *A. barbirostris bancrofti*. Other Anopheles such as *A. bironelli*, *A. longirostris*, *A. walchii*, *A. travestitus* and *A. papuae* are of no importance as vectors. *W. F. Harvey.*

Simmons (James Stevens). **Observations on the Importance of *Anopheles punctimacula* as a Malaria Vector in Panama, and Report of Experimental Infections in *A. neomaculipalpus*, *A. apicimacula*, and *A. eiseni*.—*Amer. Jl. Trop. Med.* 1937. Mar. Vol. 17. No. 2. pp. 191–212. With 5 figs. (1 map). [15 refs.]

As is well known malaria control in the Panama Canal Zone, since early days, has been largely based on a policy of anopheline species control, aiming at the elimination of *A. albimanus* and *A. tarsimaculatus*, which were considered by Darling in 1910 as the only two vectors of local importance.

A. punctimacula (*A. malefactor*) which was then, as now, very widely prevalent, has been looked upon as incapable of transmitting malaria. The hospital admission rate for malaria among Canal employees fell from 821 per thousand in 1906 to 16 in 1916, since when the rates have

fluctuated between 11 and 31. The army rates have been higher, 65·9 in 1933. The observations recorded in this paper may well explain the failure to secure any appreciable reduction of malaria incidence below the relatively low rate of 1916.

Five hundred and thirty-eight *A. punctimacula* were fed on blood containing malaria plasmodia of which 124 became infected (22 per cent.). In one group fed on blood containing 7 gametocytes of *P. vivax* per 100 leucocytes the infection rate was 56 per cent. In another group fed on blood containing from 4 to 12 *falciparum* gametocytes per 100 leucocytes the infection rate was 43 per cent. In two other groups, fed when the *falciparum* gametocyte concentration was 13 per 100 leucocytes, infection rates of 81·8 and 90·9 per cent. were noted. The author believes that *A. punctimacula* is responsible for a large part of the malaria contracted by troops in the unsanitated parts of the Zone and that as a malaria vector it may rank next in importance to *A. albimanus*. *A. punctimacula*, unlike *albimanus*, usually breeds in shaded waters.

During these experiments a specimen of *A. apimacula* was infected with *falciparum* and a specimen of *A. eiseni* with *vivax*. Thirty-one *A. neomaculipalpus* were fed on blood containing *P. vivax*: with a gametocyte count of from 4·4 to 7·8 per 100 leucocytes the infection rate was 14 per cent. When the gametocytes numbered 13·4 per 100 leucocytes the infection rate was 50 per cent. Thus of the 15 species of anophelines hitherto found in the Canal Zone no less than eight are actual or potential vectors of malaria. *N. W.*

Simitch (Tcheda). Études sur la malaria dans la Serbie du Sud. [**Malaria in Southern Serbia**].—*Bull. Office Internat. d'Hyg. Publique.* 1937. May. Vol. 29. No. 5. pp. 919–945.

The first part of this contribution has already been noted in this *Bulletin* (1937, Vol. 34, p. 373). A large part of the present instalment is devoted to a description and justification of the methods employed in evaluating the prevalence of malaria in the different parts of the territory and its variation from year to year. The author relies on the spleen index and the parasite index of school-children, which give sufficient information if certain rules be observed, the most important being that rates, to be comparable, must be based on observations made at the same time of the year, preferably September–October, the months of maximum transmission. Few will be disposed to cavil at many of the author's contentions, which are indeed generally accepted but which are, nevertheless, justified by him at very great length. The necessity for this is not clear. Spleen and parasite indexes resulting from the examination of school-children in September–October 1935 in 262 schools in Southern Serbia are presented in tabular form and give a picture of the varying degrees of prevalence of malaria in the different districts of the territory. *N. W.*

Butts (Donald C. A.). **Malaria in Camden County, New Jersey. Report of a Recent Outbreak.**—*Amer. Jl. Trop. Med.* 1937. Mar. Vol. 17. No. 2. pp. 279–287. With 5 figs.

This is a short account of an outbreak of malaria in the late summer of 1935 in Camden County, which has suffered very little from malaria in the past. Altogether 120 cases were reported. *N. W.*

Tisseuil (J.). Index paludéen chez les enfants à l'Institut Central de la Lèpre à Bamako. [**Malaria among Children in the Bamako Leper Asylum.**]—*Bull. Soc. Path. Exot.* 1937. Mar. 10. Vol. 30. No. 3. pp. 233–234.

Among sixty-four children, aged from three months to sixteen years, in the Bamako Leper Asylum in August, the spleen rate was 70 per cent. and the parasite rate 40 per cent. All infections were *falciparum*. *N. W.*

Causey (Ottis R.). **Some Anopheline and Culicine Mosquitoes of Siam with Remarks on Malaria Control in Bangkok.**—*Amer. Jl. Hyg.* 1937. Mar. Vol. 25. No. 2. pp. 400–420. [21 refs.]

During four years the author gathered information concerning the *Culicidae* of Siam, chiefly in the vicinity of Bangkok, but at intervals also in the interior of the country. The numerous breeding places of mosquitoes in Bangkok are described: the mosquito fauna of Bangkok is enormous, in spite of which there is very little malaria. Bodies of water open to free tidal flow are not breeding places of mosquitoes. Obstructed canals, because of their water-hyacinth, are less important as breeding places for anopheles than are the excavations and ditches. Cultivated rice-fields are responsible for breeding very few anophelines; uncultivated fields produce anophelines in abundance. The species of anopheline larvae captured, in the order of frequence, were:—*vagus*, *barbirostris*, *annularis*, *hyrcanus* var. *nigerrimus*, *tesselatus*, *aconitus* and *subpictus*. The most frequent species captured in light traps in houses were:—*hyrcanus* var. *nigerrimus*, *vagus*, *barbirostris* and *annularis*. Specimens of three species not found as larvae were captured as adults, *philippinensis*, *kochi* and *minimus*. Although *annularis* is generally considered to be a poor vector of malaria it is probably responsible for most of the little malaria transmission that there is in Bangkok.

An annotated list of culicines collected in Siam is contained in the paper.

When light traps were placed in the vicinity of breeding places, about equal numbers of males and females were captured; the further from the breeding place the greater the preponderance of females. It was also observed that mosquitoes, both male and female, are attracted by hot sweating animals in greater abundance than they are by cool animals. *N. W.*

Sicault & Messerlin. Sur les intoxications arsenicales chez les ouvriers employés au maniement du vert de Paris. [**Arsenical Poisoning among Workmen handling Paris Green.**]—*Bull. Office Internat. d'Hyg. Publique.* 1937. May. Vol. 29. No. 5. pp. 992–994. With 5 figs. on 4 plates.

Symptoms of arsenical poisoning were frequent in Morocco in 1936 among workmen handling Paris Green, which was used on a very large scale as a larvicide. Skin lesions were most in evidence. These most commonly appeared first of all on the scrotum, on the inner surface of the thighs and in folds of skin. A slightly oedematous erythema, which was extremely irritable, was the first sign; after three or four days minute papules and vesicles appeared in very large numbers.

Some days later the vesicles dried, forming blackish crusts. In some cases an ulcer formed on the scrotum, varying in size from a bean to a shilling piece, and generally with a corresponding ulcer on the inner surface of the thigh which was in contact with it. In two patients the papular vesicular eruption was generalized, being especially marked on the forehead, face, neck, scrotum and the folds of skin over the joints. General symptoms were little in evidence ; a third of the patients had a coryza. Only one suffered from diarrhoea. As a preventive the application of vaseline to parts of the body most exposed and most frequently implicated has much diminished the number of cases.

N. W.

Tilli (Pietro). La disinfestione calciocianamidica. Considerazioni generali igieniche e economiche. [**Calcium Cyanamide as a Larvicide.**] *Riv. di Malariologia.* Sez. I. 1937. Vol. 16. No. 1. pp. 54–59. With 8 figs. on 2 plates & 3 text figs. French summary (7 lines).

The use of calcium cyanamide as a larvicide has previously been described by the author (see this *Bulletin*, 1935, Vol. 32, p. 817). It was used extensively in the Campagna Romana, when sanctions were being applied against Italy during the Abyssinian war, with very satisfactory results. It kills eggs, larvae and pupae of mosquitoes and is equally effective against the eggs of helminths in the water or the soil. It is useful as a fertilizer. *N. W.*

McDonald (W. M.). **Malaria Control.** [Correspondence.]—*Brit. Med. Jl.* 1937. June 5. p. 1175.

This letter contains a plea for the destruction of adult mosquitoes as a valuable adjunct to anti-larval measures and a protest against its neglect. The writer considers the destruction of adult mosquitoes in houses, by swatting, fumigation and trapping, to be of great value in any campaign against malaria ; it is also cheap. *N. W.*

Boyd (Mark F.) & Kitchen (S. F.). **On the Infectiousness of Patients infected with *Plasmodium vivax* and *Plasmodium falciparum*.**—*Amer. Jl. Trop. Med.* 1937. Mar. Vol. 17. No. 2. pp. 253–262. With 4 figs.

A number of *A. quadrimaculatus* were fed daily, or every second day, on patients naturally inoculated with *P. vivax* and *P. falciparum*, throughout the clinical attacks and for some time after. Within two hours of this feeding the number of gametocyes per cubic millimetre of peripheral blood was ascertained. Fully matured infectious gametocytes of *P. vivax* are present within five days of the first observation of parasites ; they are produced, or persist, throughout the clinical attack and if the attack be longer than usual the patient remains infectious for some time after the end of the fever. Some *A. quadrimaculatus* became infected when the gametocyte density was less than ten per cubic millimeter. It appears that *vivax* gametocytes are produced at every period of multiplication, with the possible exception of the earliest divisions, until the defensive

mechanism has checked the evolution of successive parasite cycles. *P. falciparum* gametocytes are not observed till ten days after the first appearance of parasites and may not be present before the end of the primary attack. Their formation appears to be a phenomenon terminal to the completion of five or six cycles of trophozoite multiplication. No infection of *A. quadrimaculatus* was obtained with submicroscopic densities of *falciparum* gametocytes and densities less than 100 per cubic millimetre generally failed to infect. In *A. quadrimaculatus*, *vivax* gametocytes are about ten times as effective as are *falciparum* gametocytes. *N. W.*

Boyd (Mark F.) & Kitchen (S. F.). **A Consideration of the Duration of the Intrinsic Incubation Period in Vivax Malaria in Relation to Certain Factors affecting the Parasites.**—*Amer. Jl. Trop. Med.* 1937. May. Vol. 17. No. 3. pp. 437–444.

In 180 successful inoculations of *vivax* malaria out of 182, the number of days elapsing from inoculation to the first microscopical detection of parasites varied between 8 and 23, mean 13·22. The length of the incubation period did not appear to be influenced by either the length of the intrinsic incubation in the source of infection, the period of the primary attack in the source of infection at which mosquitoes were infected or the duration of the extrinsic incubation period in mosquitoes. It appeared to be influenced inversely, however, by the number of sporozoites inoculated as indicated by the number of mosquitoes used. The varying susceptibility of human hosts appears to be more important in determining the length of the incubation period than any discernible factors modifying sporozoites. *N. W.*

Nauck (E. G.). Ueber Malariatodesfälle bei Seeleuten. [**Fatal Cases of Malaria in Seamen.**]—*Deut. Med. Woch.* 1937. May 14. Vol. 63. No. 20. pp. 774–775.

A German steamer put into Lagos for 4 days, during which time the crew went ashore a great deal. On the return journey to Germany about 8 to 10 persons became ill with what was finally determined to be a malarial infection and 4 of these died. The author discusses the causes which led to the late recognition of these cases with fatal results. 1. The unsatisfactory and insufficient prophylaxis. He considers that the best results would have been got by giving atebrin after leaving Lagos, in therapeutic doses, 0·1 gm. thrice daily for 5 days. 2. Overvaluation of the preventive measures as carried out by the ship's doctor or officers. The conception that quinine prophylaxis can prevent malarial infection if given *only* during the stay in the infected area is a dangerous one. Quinine is not a causal prophylactic and only delays the appearance of the symptoms, but not the infection. 3. Illness after disembarkation or during leave. The delay of the illness caused by insufficient prophylactic treatment had these unsatisfactory results, the patients treated themselves in their houses, called in the doctor late and delayed their admission to hospital for specific treatment. 4. The simultaneous occurrence of an influenza epidemic. This led to the cases being misdiagnosed. 5. "Atypical" course. Mühlens has repeatedly pointed out that the primary

infection with malaria is seldom typical, and it is liable to be confused with influenza, meningitis, typhoid and other infectious diseases, especially by doctors who have not had tropical experience. The spleen may not be enlarged. 6. Omission of blood examination. In illnesses of seaman, not only on board ship, but also in their houses, blood examination should invariably be undertaken. Should blood examination not be possible, every case with fever in seamen would be better treated as one of malaria in order to prevent the fatal issue. He concludes by stressing the great importance of giving ship doctors instruction in the problems of malaria on board ship.

E. D. W. Greig.

Séno-Sastroamidjojo (R.). Nephritis bij malaria tropica. [**Nephritis in Malaria.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1937. Apr. 20. Vol. 77. No. 16. pp. 984–996. [32 refs.]

Acute nephritis is not a commonly observed symptom in malaria. The author describes two cases with infection of subtertian, tropical, malaria in which this was a prominent feature. There was albumen in the urine, blood and casts in the urinary deposit, and tropica rings in the blood. All these symptoms disappeared under ordinary treatment for the malarial condition. *W. F. Harvey.*

Yung Tsü (T.). Ein Fall von Malaria-Polyarthritis. [**Case of Malarial Polyarthritis.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. June. Vol. 41. No. 6. pp. 462–463.

The author describes a case of malaria accompanied with symptoms of acute rheumatic polyarthritis. Benign tertian parasites were found in the blood. With antimalarial treatment the patient was clinically cured. An editorial note at the end of the paper states that in their opinion the apparent therapeutic success and the single find of benign tertian parasites does not justify the conclusion that the malarial infection was the cause of the rheumatic attacks.

E. D. W. Greig.

Matsunobu (M.). Beiträge zur Hämatologie der Malariakranken. I. Mitt. Ueber die osmotische Resistenz der Erythrozyten. [**On the Osmotic Resistance of Red Corpuscles in Malaria Patients.**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1937. May. Vol. 36. No. 5 (386). [In Japanese pp. 992–1001. With 10 charts. [15 refs.] German summary p. 1002.]

The author has investigated the fragility of red cells in parallel with reticulocytosis in malaria patients in the febrile stages. Enumeration of reticulocytes was made by the Nile blue method. Fourteen subtertian infections were studied; on thirteen occasions in the stage of fever, on six after natural fall of temperature, and all fourteen after treatment with atebrin and plasmoquine three on the same day and eleven a week later. Six healthy subjects served as controls. It was found that usually in the fever stage the erythrocytes were more resistant to hypotonic saline than were either the controls or the

afebrile malaria patients. Occasional exceptions were observed. When the temperature became normal, whether the result of treatment or not, the resistance generally became normal, but several times considerable departures from the normal, both above and below, were seen. No parallelism was observable between the osmotic resistance and the fluctuations in the reticulocyte counts. *H. H. S.*

CORRADETTI (Augusto). Sul significato di un reperto di plasmodi con diverso grado di sviluppo nello stesso globulo rosso. [**Significance of Plasmodia at Different Stages of Development in the Same Red Cell.**]—*Riv. di. Parassit.* Rome. 1937. Apr. Vol. 1. No. 2. pp. 169–171. With 4 figs. on 1 plate. English summary (4 lines).

The author records and illustrates the existence of malaria parasites at markedly different stages of development in the same red cell. For instance, a red cell containing a mature *vivax* gametocyte harboured also a merozoite. The contention that red cells are susceptible to plasmodial invasion in the reticulocyte stage only is ill-founded. This is the conclusion that the author draws from his observations. *N. W.*

VENOMS AND ANTIVENENES.

KOHLSHÜTTER (E.) & MINNING (W.). Ein Fall von Spättod nach Biss der südamerikanischen Viper *Lachesis alternatus*. [**Late Death after Bite by the South American Viper** *Lachesis alternatus*.]—*Deut. Med. Woch.* 1936. Dec. 11. Vol. 62. No. 50. pp. 2043–2047.

The poison of *Lachesis alternatus* contains haemorrhagin and thrombase but no neurotoxin. Haemorrhagin is a cytolysin, destroyed by heating at 75°C. for 30 minutes and precipitated by alcohol. It has been proved experimentally that the haemorrhage which takes place from its action is due to lysis and rupture of the capillary endothelium and that this occurs not only at the site of the bite but also throughout the whole body. Cramps, which are an early symptom of viper bite, are the result of small haemorrhages into the brain. Thrombase is abundantly present in the *Lachesis* poison. It acts firstly upon fibrinogen to produce coagulation but also upon the fibrin proteolytically. Thus, if the concentration of thrombase is large, no coagulation at all occurs, for fibrin is immediately dissolved. The course of events after a bite is of this description: First, an extensive local thrombosis and a haemorrhagic necrosis, then a solution of the fibrin, which allows the haemorrhagin to act upon the capillaries to destroy them. As a result continuous oozing of blood, which does not clot, takes place at the bite.

Clinically, severe pain develops at the bite which may become unbearable in the course of the next few hours. This is followed by weakness, sleepiness, extremely subnormal temperature and long continued vomiting. Consciousness is never lost except in very severe cases. Vasomotor paralysis occurs on the 2nd or 3rd day and at this stage death may occur. Diffusely distributed subcutaneous and mucosal haemorrhages complete the picture. If recovery takes place it will be found that the region of the bite shows vesicles with sanguineous contents and extensive necrosis. Infection may take place and may lead to loss of fingers or toes or even of hand or foot.

The only treatment is the injection of the specific serum. No removal of any sufficient amount of poison can be effected and therefore the popular methods of sucking the wound, cauterizing it or even cutting it out are rather superfluous. Even ligature of the limb affected is to be abandoned. What is satisfactory, however, is to produce a degree of stasis by Bier's method. There is no place in the treatment of snake bite for the use of alcohol. It may stimulate for the moment, but this is quickly followed by its paralytic action which will help to promote absorption of the poison.

It has been established that the various antisera are strongly specific in respect of the various toxic elements in a poison and that there is no serum with universal action against all snake poisons. A fortunate circumstance is that an antiserum does not lose potency with age.

There follows this general description of the effects of a bite a detailed account of symptoms, treatment and post mortem findings in a particular case in which an animal keeper had been bitten and survived the bite for 8 days, which is much longer than the 3 days which, it is stated, is the limit for *Lachesis* bite. *W. F. Harvey.*

Dobreff (Minko). Ueber die Giftschlangen in Bulgarien. Zugleich ein Beitrag ueber einen Todesfall infolge eines Giftschlangenbisses. [**Venomous Snakes in Bulgaria. A Fatal Case of Snakebite.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. May. Vol. 40. No. 5. pp. 197–200. With 4 figs.

There is a rich snake fauna in Bulgaria ; of the 28 species of snakes found in Europe 15 are met with. Four of them are poisonous : *V. ammodytes* (Sand viper) ; *V. berus* (adder, Höllennatter) ; *V. aspis* and *V. ursinii* (long-headed adder). Of these, the first is the most common and occurs all over Bulgaria ; there are three subspecies found : *V. ammodytes ammodytes* ; *V. a. meridionalis* and *V. a. montandoni*, all in the plains up to 800 metres above sea level. *V. berus* is the most venomous and lives in the mountainous districts to 2,700 metres, very rarely is it present in the plains. The black variety, *V. berus* var. *prester* is also found. The other two snakes are uncommon and resemble in many respects *V. berus*. Good photographs of the four kinds are reproduced.

Beyond the fact that cases of snakebite are far from rare in Bulgaria, nothing definite is known; there are no statistics. The author records the case of a child of 3 years bitten on the right ankle by a (?) *V. berus*. A ligature was applied at once, but removed shortly after. Nothing else was done, and the father " waited for the train " and took the child to a chemist 4 hours after in a stuporous condition. He had no antivenene but injected round the site 1 per cent. solution of potassium permanganate ; alcohol, adrenalin, caffein and camphor were also tried, but death took place 6 hours after the bite ; the child did not regain consciousness. *H. H. S.*

Peck (Samuel M.), Rosenthal (Nathan) & Erf (Lowell A.). **The Value of the Prognostic Venom Reaction in Thrombocytopenic Purpura.**—*Jl. Amer. Med. Assoc.* 1936. May 23. Vol. 106. No. 21. pp. 1783–1791. With 2 figs.

Observation of 50 patients, 14 males and 36 females, forms the basis of this study. All were clinically typical, exhibiting a haemorrhagic tendency—purpura, ecchymoses, bleeding from mucosae—diminution of platelets, prolonged bleeding time and absence of clot retraction. Forty-four were so-called idiopathic, *i.e.*, the cause was not determined.

The prognostic reaction consists in the intradermal injection of 0·1 cc. of a 1 : 3,000 standardized moccasin venom (and a control of physiological saline) ; the result is read after an hour, though there may be a delayed reaction after 12 hours. A positive is indicated by capillary rupture and local diffusion of blood. For prognosis a series of tests must, of course, be made. A solitary test, if positive, merely indicates the existence of a purpuric state and capillary fragility ; continuance of a positive is, therefore, a bad sign, a reversal to negative is of good prognostic value. In 2 out of 8 cases the result was insistently positive ; these ended fatally. If the patient is refractory to treatment by the venom and the reaction is at the same time persistently positive, this is regarded as calling for splenectomy. Eight came within this category ; one recovered, two others improved, and in all three the venom test was reversed. In three there was no benefit ; the purpuric condition remained and the venom test persisted positive, and death occurred. *H. H. S.*

SERGENT (Etienne). Action thérapeutique de l'injection sous-cutanée d'eau contre les accidents dus aux venins. [**Injection of Water in the Treatment of Venom Effects.**]—*Ann. Inst. Pasteur.* 1936. Aug. Vol. 57. No. 2. pp. 127–133. With 3 figs.

Two series of experiments are reported, the first with the venom of *Cerastes cornutus* [see also this *Bulletin*, 1936, Vol. 33, p. 400], the second with scorpion venom, *Buthus occitanus* and *Prionurus australis*.

In the first, 577 mice were injected with a dose of the viper venom which killed under ordinary conditions in two hours. The mice were divided into four groups: the first served as controls and all died; the second group of 151 received soon afterwards 10 drops of an antivenene prepared against vipers of North Africa, and 39 per cent. survived, in 56 per cent. death was delayed, the remaining 5 per cent. died in two hours, like the controls. A third group (of 101) received 10 drops of European viper antivenene; 34 per cent. survived, in 56 per cent. death was retarded, 10 per cent. died in the two hours. The fourth group (151) received injections of 10 drops of physiological saline; the corresponding percentages were 16·5 survivals, 67 death delayed, 16·5 fatal in two hours. From the figures it is seen that the European antivenene is less potent that the North African, while the saline is also protective to a degree about half that resulting from the European serum.

Experiments on the same lines were carried out with the scorpion venoms; 602 mice receiving an injection fatal in two hours in the untreated. Of these, 204 served as controls and all died within the specified time; another 398 were given 10–20 drops in either water, physiological saline, adder serum or frog serum, and 8 per cent. survived, 35·9 per cent. died in two hours, and in the remaining 56 per cent. the fatal results were delayed.

Next, the author set out to test whether the inhibiting effect was due to the water itself or to the salt content. Thirty-one mice were given 10 drops of 5 per cent. NaCl after injection of a fatal dose of the scorpion venom, 26 survived; another 34 were given distilled water in place of the saline and 30 survived (84 and 88 per cent. respectively). Hypertonic salines were less satisfactory than the 0·9 per cent.

Following up these results, the author went on to determine whether the effect was due merely to dilution of the venom before the latter had time to act upon the body cells. 678 mice were divided into six lots of 113 each: to all was given a mortal dose of Cerastes venom, but to group I this was mixed with two drops of the saline, to group II with four drops, to groups III, IV and V, eight, sixteen and thirty-two drops respectively, while to group VI were given, a few minutes after the injection of the venom, ten drops of the saline in a different part of the body. The results were somewhat anomalous; groups I to IV showed an average length of survival proportional to the degree of dilution of the venom, *viz.* 2¼, 4, 4½, and 11¼ hours, but group V, with the 32 drop dilution, survived on an average 2½ hours, or practically the same as group I, with two drops. Of this first lot 5 only survived (0·8 per cent.), whereas of group VI where the saline was injected in a different part of the body 31 survived or 27·4 per cent. and in those which died the average length of life was 13 hours. In other words, the saline was more efficacious when it was injected after the venom than when venom and saline were mixed before injection.

If, therefore, specific antivenene is not at hand, death may be delayed and perhaps averted by injection of physiological saline into a man or animal bitten by Cerastes or stung by a scorpion. Its use is also indicated for hyperimmunization of animals from whom the antivenenes are being prepared. *H. H. S.*

GRASSET (E.) & ZOUTENDYK (A.). Recherches sur le venin et l'anavenin de la vipère du Gabon (*Bitis gabonica*). Importance de l'introduction de son antigène dans la préparation du sérum antivenimeux pour l'Afrique équatoriale. [**Study of the Venom of** *Bitis gabonica* ; **the Need for its Inclusion in preparing Antivenenes for Snakes in Equatorial Africa.**]—*Bull. Soc. Path. Exot.* 1936. Feb. 12. Vol. 29. No. 2. pp. 210–217. [10 refs.]

Bitis gabonica is the largest of the African vipers, the length being from 3 to 6 feet. The venom for this study was obtained from adult specimens captured in Mozambique and kept in captivity for over a year. The venom in the dry state contains 9·6 per cent. of protein ; it is readily soluble in water or physiological saline. Its toxicity was tested on mice, rats, guineapigs, rabbits, pigeons, fowls and sheep and compared with the venoms of *B. arietans*, *B. atropos* and *B. caudalis*, by intravenous or subcutaneous injection. A protocol gives details of these findings and comparisons. The important point for us at present is that the toxicity of the *B. gabonica* venom was much less than that of *B. arietans*, but was much more powerfully haemostatic. A haemophilic blood whose coagulation time *in vitro* was 25 minutes clotted with 1 in 10,000 *gabonica* venom in 5–6 minutes, whereas with the same proportion of *B. arietans* venom the blood remained uncoagulated after an hour's contact [it would appear, therefore, to retard coagulation].

The author next prepared an anavenin by addition of 0·75 per cent. formol and keeping the mixture at 37°C. After 5–6 weeks the product was practically atoxic, rabbits being unaffected by the equivalent of more than 10 m.l.d. of the original venom. Experiments at cross immunization with *B. arietans* showed that immunity due to *gabonica* anavenin is protective equally against *arietans*, whereas that due to *arietans* while highly potent against its own venom will not protect against even 2 m.l.d. of *gabonica* venom. In fact none of the antivenenes of other African vipers proved protective against *B. gabonica* venom and therefore the latter should be included in the preparation of the polyvalent product for use in Africa [see also this *Bulletin*, 1936, Vol. 33, pp. 382, 383]. *H. H. S.*

GRASSET (E.) & ZOUTENDYK (A.). Préparation d'un sérum antivenimeux contre le venin de la vipère du gabon (*Bitis gabonica*). [**Preparation of Antivenene for** *Bitis gabonica*.]—*C. R. Soc. Biol.* 1937. Vol. 124. No. 7. pp. 609–612.

Antivenenes against the common African viperidae venoms are ineffectual against that of *Bitis gabonica*, although the reverse does not obtain, for *gabonica* antivenene is active against *B. arietans*, for example. It is essential therefore to include the former in antisera for use in equatorial Africa.

By injection of horses with the anavenin in doses from 50 to a maximum of 700 mgm. in 9 injections at weekly intervals, a serum was obtained of which 1·0 cc. neutralized 3·3 mgm. venom. By fractional precipitation concentration was obtained and 0·45 cc. of pseudoglobulin neutralized 5 mgm. of the venom. 3 cc. of the unconcentrated or 1·2 cc. of the concentrated, pseudoglobulin, serum neutralized 5 mgm. of *B. arietans* venom. Probably with more prolonged injection of the horses with larger doses a still more potent antivenene could be obtained.

By experiment an average of 200 mgm. venom can be extracted by pressure on the *B. gabonica* glands ; if it be assumed that half to two-thirds of this is injected then 20–30 cc. of the antivenene should suffice in treatment of human cases. *H. H. S.*

GRASSET (E.) & ZOUTENDYK (A.). **The Antigenic Characteristics and Relationship of Viperine Venoms based on the Cross Neutralizing Action of Heterologous Antivenomous Sera.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Nov. 28. Vol. 30. No. 3. pp. 347–354. [10 refs.]

The question of therapeutic cross-action is one of great importance to those preparing polyvalent antivenenes, because the Viperidae are so diverse and their venoms not well defined. The authors have experimented with the following venoms : *Vipera aspis* of Europe ; *Cerastes cornutus* (North Africa) ; *Bitis arietans, B. gabonica* and *Causus rhombeatus* (South and Equatorial Africa) ; *V. russelli* (India), *Ancistrodon rhodostoma* (Java) ; *Crotalus terrificus, Lachesis atrox* and *L. jararaca* (Brazil), and antisera from various institutes. For South American venoms pigeons were employed, for the others rabbits, the mixture of venom and antivenene being allowed to remain at laboratory temperature for an hour before injection. The results are presented in tables, of which that correlating the details is shown on p. 724. Some difficulty arises from the fact that the sera are standardized by workers in different parts of the world who have not all the same view regarding the test dose of venom, the temperature at which the venom-antivenene mixture should be kept, the animal to be used for test, etc. The results show that antigenic relationships of viperine venoms cannot be based on zoological grounds nor on geographical distribution (see above), whereas, on the other hand, relationship is observed where both zoological grounds and geographical distribution would least lead one to expect them. It is impossible, state the authors, in the present state of our knowledge, to differentiate between "specificity" and "similarity." *H. H. S.*

MALLICK (S. M. K.). **The Use of Tapioca in Immunization with Snake Venoms.**—*Indian Jl. Med. Res.* 1936. Apr. Vol. 23. No. 4. pp. 993–996.

The ordinary method, employed in past years at the Central Research Institute, for obtaining antivenene to Indian cobra and Russell's viper has been to inject horses with increasing doses of the two venoms at 10-day intervals. In most cases it was found necessary

The Cross Action exerted by the Various Antivenomous Sera Tabulated in a Comparative Form.

Serum	Venoms									
	Europe	North Africa	Equatorial and South Africa			Asia		America		
	V. aspis	*C. cornutus*	*B. arietans*	*B. gabonica*	*C. rhombeatus*	*V. russelli*	*A. rhodostoma*	*C. terrificus*	*L. atrox*	*L. jararaca*
Pasteur Institute, Paris, "A.N." serum ...		Specific ++++	O	O	O	O	+++	+	+++	+
Pasteur Institute, Paris, "E.R." serum	Specific ++++		O	O+	O	++	+++	+	++	+++
Research Institute, Kasauli, India	+++	++++	O+	+	+	Specific ++++	+++	+	+++	++++
South African Institute for Medical Research, Johannesburg ...	O	+++	Specific ++++	O+	Specific ++++	O	++++	+	+++	++
Instituto Vital Brazil, Anti-crotalica serum	++	O	O+	O	O	O	++++	Specific ++++		
Instituto Vital Brazil, Anti-bothrops serum	+++	++++	O+	O	O	O	+++		Specific ++++	Specific ++++
Pasteur Institute, Bandoeng, Java	O	O	O	+	O	O	Specific ++++	+	++++	++++

NOTE :—O = no demonstrable neutralizing value. O+ = feeble and ill defined cross-neutralization. +, ++, +++, ++++ = increasing degrees of definite cross action, the last being approximately equivalent to a neutralization of specific therapeutic value.

to advance to doses as high as 100 mgm. of each venom and a total of 300–400 mgm., taking about 4 months (it might be even longer) to attain the required degree of immunization. The results of adding tapioca or an absorbent aluminium hydroxide to the venoms have been studied. With tapioca the total amount of venom required was only one-third of the former quantity, though the time was not much shortened—3 months. Also, local abscesses, which were frequently seen under the old method, were much fewer. Again, under the older method, after the horse had been rested, as much as 150 mgm. of each venom might be needed to bring the antivenene up to titre, whereas with tapioca 40–50 mgm. sufficed. In the case of daboia venom, though there had not formerly been any difficulty in obtaining a high anti-venene under the old method, the use of tapioca proved very advantageous. Comparative tests were carried out with goats. The addition of tapioca gave more satisfactory results than did aluminium hydroxide. *H. H. S.*

HANUT (Charles Joseph). A propos de la spécificité des sérums antivenimeux. [**The Specificity of Antivenenes.**]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 27. pp. 271–273.

HOUSSAY and SORDELLI have shown that the neutralization of the coagulant action of crotaline venoms by their corresponding anti-venenes is to a certain extent specific; CÉSARI AND BOQUET have studied quantitatively the analogous actions of the antivenenes of *V. aspis*, *C. cornutus* and *Naja tripudians* and have found some lack of specificity in the first two in spite of their close relationship. The action of cobra antivenene, whether it reacts with these and whether the reciprocal action occurs, has not been determined.

The author has therefore investigated the coagulant or anti-coagulant actions of various venoms, and of antivenenes of aspis, cobra, cerastes and bothrops (prepared from several Brazilian Bothrops). The results are presented in the form of a table from which it is seen that the action is in general specific, the chief departure being the anticobra serum, which is more potent against the venom of *B. nummifera* than that of *N. tripudians*. The author can suggest no explanation for this at present. Other exceptions may be due either to zoological affinity or to analogy of mode of action; *e.g.*, aspis antivenene has some effect on the coagulation due to Cerastes venom and *vice versa*. At first sight it seems strange that antibothrops serum should reduce the coagulative action of Cerastes, yet have no such action on that of *V. aspis*, but the following will account for this: In the presence of calcium Cerastes venom coagulates, just like that of Bothrops, solutions of fibrinogen, but the venom of *V. aspis* does not. Further, in contradistinction with Bothrops venom, neither that of *Cerastes* nor that of *V. aspis* coagulates re-calcified plasma. "If the anti-aspis, anti-cerastes and anti-cobra sera inhibit the coagulant effects of *B. nummifera* venom, but not that of *B. atrox*, this is doubtless due to the very marked coagulative properties of the last, which exceeds considerably that of *B. nummifera* venom."

To sum up: We may be right in stating in a general way the law of specificity of antivenenes to counteract the coagulant action of venoms, but there are important exceptions, some of which find an explanation in zoological relationship. *H. H. S.*

César (E.) & Boquet (Paul). Recherches sur les antigènes des venins et les anticorps des sérums anti-venimeux. (Quatrième mémoire.) Action d'un sérum antivenimeux bivalent (*Bitis arietans* + *Sepedon haemachates*) sur les deux venins homologues et divers venins hétérologues. [**Antigens of Venoms and the Antibodies of Antivenomous Sera. IV. Action of a Bivalent Antivenene on the Homologous and Heterologous Venoms.**]—*Ann. Inst. Pasteur.* 1937. Jan. Vol. 58. No. 1. pp. 6–25.

Snake venoms may be regarded as composed of several antigenic elements and the same elements may be contained in the venoms of different species of snakes. This conception leads to the hope that by means of a mixture of venoms an antivenene might be obtained which was polyvalent. In this study, which is one of a series [see this *Bulletin* 1936, Vol. 33, p. 384], an antivenomous serum was obtained from horses immunized with the viperine venom of *Bitis arietans* (the puff-adder) and that of the colubrine snake *Sepedon haemachates* (the ringhal). In the tests the antitoxic power of the mixed serum was measured *in vivo* and the antidiastatic power *in vitro* against venoms of (1) Viperidae, *Bitis arietans*, *Vipera aspis*, *Cerastes cornutus* and *V. russelli*, (2) Crotalinae, *Crotalus terrificans* and *Bothrops atrox* and (3) Colubridae, *Sepedon haemachates*, *Naja tripudians* and *N. flava*. Each of these venoms was first investigated for its toxicity, coagulant or anticoagulant power and haemolytic power. The mixed antivenomous serum was tested for its antitoxic, anticoagulant, anti-anticoagulant and antihaemolytic properties.

Two horses, Nos. 905 and 917, were utilized for production of the antisera. They were, for upwards of a year, treated every 15 days with subcutaneous injections of a mixture of the test venoms. Thus horse 905 received, in all, 12·107 gm. *B. arietans* venom and 8·069 gm. *S. haemachates* venom. The rabbit was the test animal and the mixture of the antiserum with either a homologous or a heterologous venom was, after 30 minutes at 37°C., injected intravenously for the testing of antitoxic potency. Both of the horse antisera were found to be antitoxic not only to their homologous venoms but also, in some degree, to the heterologous venoms. Serum 905, the most active of the two against *B. arietans* venom had also a stronger potency than serum 917 against the other viperine venoms. On the other hand serum 917, which was the more antitoxic against *S. haemachates*, was also more antitoxic towards the other colubrine venoms. Curiously enough both sera were more antitoxic to the heterologous *N. flava* venom than to the homologous *S. haemachates* venom. Both antisera had little or no neutralizing action against the crotaline venoms of *C. terrificus* and *B. atrox*.

As regards the other properties investigated:—(1) The anticoagulant power of the antisera was qualitatively similar to the antitoxic power, but not completely so, in a quantitative sense. (2) The same relationship held for anti-anticoagulant action and antitoxic power. (3) A much greater divergence from parallelism, amounting to absence, was found in the relationship between antihaemolytic power and antitoxic power of the two antisera.

Thus these experiments confirm previous conclusions as to the "want of co-ordination between the antitoxic and antidiastatic properties of antivenomous sera" and "condemn definitely those methods of titration which are based on the determination of their

action on the coagulation of plasma or the haemolysis of red cells by venoms." The antigenic constituents of most of the venoms reveal serological relationships between snakes which are in no sense zoological or geographical. It would seem, too, from these experiments that the *Crotalinae* are as different from the *Viperidae* as are the *Colubridae*. It is suggested that by careful choice of venoms for mixed immunization, antisera may at least be obtained for use against all forms of snake bite in certain definite regions, say, that of a continent. *W. F. Harvey.*

DEY (A. C.). **A Case of Scorpion Bite.**—*Indian Med. Gaz.* 1936. July. Vol. 71. No. 7. pp. 402–403.

It is rare for scorpion sting to be fatal and the case here reported is of additional interest because recovery seemed to have taken place when fresh symptoms set in which had a fatal issue within 24 hours of the infliction of the sting.

The patient was a girl of 11 years, stung on the left breast and on the chin. An hour later she was restless and perspiring, complained of burning pain at the sites stung, and was frothing at the mouth. On being brought to hospital she was in a state of shock, temperature 96°F., pulse 145, heart sounds feeble, pupils dilated, eyes congested, tongue dry. The same evening there was much improvement and the child passed a fairly good night, and seemed well in the morning, but later became restless, vomited some blood about 10 a.m. and passed a stool containing blood; respiration rate increased to 45, and the pulse to 160 per minute and death occurred in a little over an hour. Colonel CHOPRA adds a note on scorpion poisoning and on the venom.

H. H. S.

SERGENT (Etienne). Piqures de scorpion en Algérie (1934). [**Scorpion Sting in Algeria.**]—*Arch. Inst. Pasteur d'Algérie.* 1936. Mar. Vol. 14. No. 1. pp. 53–61. With 1 fig.

This article is in itself very condensed and hardly permits of abstract. Scorpion stings vary greatly in the severity of the symptoms they provoke in different parts of Algeria; in some districts (7 are mentioned by name) they have caused death, not only in children but in adults also, whereas in others the results are comparatively mild. Fatal cases are recorded every summer in Tiout (Oran Departement), Ain Boucif, Bou Saâda and Mzab (Algiers), and Biskra, Touggourt and Ouargla (Constantine); in 9 other places fatalities are occasionally recorded. A list is given of 51 areas where stinging is reported, but no fatal cases, and another of 39 areas whence no cases have been reported. The species met with are: *Heterometrus maurus*, which is very common but does not cause serious symptoms; *Buthus occitanus*, also very common and exceptionally causes death in children; *Prionurus aeneas* and *P. liouvillei* are two black varieties, but no fatal results have been recorded from their poison, in spite of the widespread belief that it is the black scorpions which cause death; *P. australis* has a potent toxin, some 20 times that of *B. occitanus*, and is accredited with several deaths each year, in fact it is this species which is responsible for most of the fatalities. *H. H. S.*

SERGENT (Eteinne). Obtention d'un sérum actif contre le venin de scorpion. [**Preparation of Scorpion Antivenene.**]—*C. R. Acad. Sci.* 1936. Mar. 16. Vol. 202. No. 11. pp. 989–990.

——. Préparation d'un sérum contre le venin de scorpion.—*Ann. Inst. Pasteur.* 1936. Sept. Vol. 57. No. 3. pp. 240–243.

In Algeria deaths from the sting of the scorpion, *Prionurus australis*, are not uncommon. The author therefore set about preparing an antiserum from the ass, this being a very susceptible animal. Preliminary investigations determined that the lethal dose for mice was one-fortieth of a telson (terminal segment of the scorpion). The telson was used because it was found practically impossible to obtain the poison in ponderable amount. The amount in individual telsons varied, so a large number were pooled and the venom for injection prepared thus :

The telsons, removed during life, are kept at 37°C. till dry, then in the dark in sealed tubes at 15–22°C. One hundred and two were ground in a mortar with 2 cc. of 0·9 per cent. physiological saline, and the resultant mass diluted with 64 cc. saline. After centrifugation, the opalescent fluid is decanted into a sterile flask, 34 cc. of neutral sterilized glycerin added and the mixture kept at 37°C. for 15 days ; it is then ready for injection. The fatal dose for a mouse is half a drop in 5 drops of saline.

As little as one-tenth of a telson may kill an ass, so the immunization has to proceed very cautiously. Starting with one drop (= 1/20 telson or 2 mouse m.l.d.) injected subcutaneously the dose is gradually increased at 3–4 day intervals, ceasing for a time if there is rise of temperature or loss of weight. After 7 or 8 injections, *i.e.*, having reached about 20 drops, the venom is more highly diluted for injection, and after the higher injections, equivalent to 5 telsons, intervals of 2–3 weeks are allowed to elapse and the animal is bled. In 12 months a serum of considerable potency was obtained. Of 208 mice receiving a fatal dose and 10 drops of the antivenene 173 survived (83 per cent.), whereas 76 controls all died. In another series 17 survived out of 18 receiving 3 m.l.d. and 10 drops of the serum. It was found equally efficacious against other scorpion venoms ; nine out of ten survived after injection with the poison of the yellow scorpion (*Buthus occitanus*) and the black scorpion (*Pr. liouvillei*). For man the dose suggested is 20 cc. at least. *H. H. S.*

D'AMOUR (Fred E.), BECKER (Frances E.) & VAN RIPER (Walker). **The Black Widow Spider.**—*Quarterly Rev. Biol.* 1936. June. Vol. 11. No. 2. pp. 123–160. With 7 figs. [13 refs.]

Latrodectus mactans, the Black Widow, Hourglass, or Shoebutton spider, is found throughout almost all the United States, parts of Canada, Central and South America as far as Peru, and the West Indies. The authors believe that they have good evidence that it is increasing greatly in numbers in the United States ; at times it is so numerous that the grape-pickers in Colorado refuse to work in the vineyards. According to Emil Bogen, five per cent. of the spider bites cause fatal results in man. He has described the symptoms as they occur in human beings (*Ann. Intern. Med.*, 1932). The bite is not painful, but it is followed by a dull numbing pain, which ascends from the extremity bitten, and then becomes localized in the muscles of the chest, back and abdomen ; this pain is very severe. The abdominal wall becomes rigid, and respiration is impeded by spasms of the

thoracic muscles. The blood pressure rises, and there is often nausea and vomiting; there is also slight fever and leucocytosis. These symptoms appear within four hours, and may last for two or three days. In fatal cases death occurs in 18–36 hours. [See also this *Bulletin*, 1936, Vol. 33, p. 401.]

The Black Widow is a small spider; the length of the female, which is about four times the size of the male, is 1 to 1·5 cm. The pair of poison glands lie superficially under and behind the ocular region of the cephalothorax. Each gland is 1–2·5 mm. in length, and weighs 1·5–2 mgm. The life cycle of the female appears to last a little more than a year; that of the male is shorter.

The female produces from 1–4 egg sacs, each containing on an average 140 eggs.

The authors obtained the venom by macerating the poison glands in salt solution; young rats, 50–60 gm. in weight, were used in the experiments. The amount of dried venom obtained from each spider was, on an average, 0·126 mgm. The "average lethal dose," that is the amount of venom which will kill fifty per cent. of rats, is one-fourth of the venom yielded by one spider. The injections into the rats were all given intraperitoneally; the spiders used were all mature females, as indicated by the absence of any markings on the dorsal surface.

A few experiments were made to determine the toxicity of immature females and male spiders; the venom of six immature females caused symptoms in the rats, which however all recovered; the venom of twelve males caused practically no symptoms.

When a spider bites another of the same species, the latter is immediately paralysed, but may recover after several hours.

The venom of the mature female is extremely potent; the authors found that 1 mgm. of rattlesnake venom (*Crotalus albicans*) was required to kill ninety per cent. of the rats; the same result was caused by only 0·064 mgm. of Latrodectus venom. The eggs of the spider are also highly toxic; they contain some poisonous material which is also found in the tissue fluids of the spider. It was found that 1000 eggs weigh 640 mgm. and yield, on maceration in distilled water, filtering and drying, 100 mgm. of a pale yellow, flaky precipitate. The dried venom of the glands, and the dried precipitate from the eggs showed little, if any, diminution in toxicity after being kept for seven weeks. The toxic material in the eggs is neither a lipoid nor an alkaloid, but is probably a globulin, or associated with globulins.

The venom in the poison glands is highly labile; the glands, macerated in distilled water, yield a filtrate which gives positive reactions for protein. When subjected to dialysis, the concentrated dialysate caused no symptoms; while the equivalent of half a spider of the non-dialysable residue killed 87 per cent. of the rats. Though various precipitating agents were tried, it was not found possible to separate the protein from any other non-dialysable substance.

S. C. Liu and H. Wu reported (*Chinese Journ. of Physiology*, Vol. 8, 1934) that methyl alcohol can precipitate proteins without causing denaturization if the length of time does not exceed four hours. The venom glands of 40 spiders were macerated in 10 cc. of distilled water. One cc. of this was used as a control; 4 cc. of the remainder were treated with 100 cc. of absolute methyl alcohol, and left in the refrigerator for three hours. A white precipitate was formed, quickly dried, and dissolved in saline. Another 4 cc. of the venom solution

was treated in the same way, but only left standing for one hour. The filtrate from these solutions was evaporated to a small volume. In the rats which received the protein precipitate paralysis of the legs set in early, and was as severe as in animals receiving ordinary venom. But the animals showed no general depression, no respiratory symptoms, no affection of the lachrymal glands, and no sanguineous discharge from the nostrils, such as occur when ordinary spider venom is administered: recovery from the paralysis occurred within a few hours. It seems likely that there are two factors present in the venom, one of which, the more lethal, is destroyed by alcohol, while the other factor is not affected.

When the venom is given by the mouth, no symptoms of poisoning follow. Both pepsin and pancreatin were found to destroy the toxicity of the venom; so, too, do weak acids and bases. Boiling for five minutes, and exposure to 75°C. for 20 minutes, completely destroyed the toxicity, but it was not affected by exposure to 37°C. for six hours.

An attempt was made to immunize 26 rats, of which 10 were mature and 16 immature. The full-grown rats were given a quarter of the venom of a spider twice a week for three weeks, then half twice a week for two weeks; the young rats received smaller quantities of venom spread over the same period of time. Then all the animals were given an injection of one spider's venom. Of the adult rats, all showed symptoms of poisoning, but recovered; of the 16 immature rats all showed symptoms, and 6 died. Thus it seems that little, if any, immunization had occurred.

The survivors were injected for a further period of five weeks, and were then given the equivalent of one spider each: no symptoms followed. Three days later they were given two spiders each, and again, three days later, four spiders each; no symptoms whatever followed. It appears therefore that the rats had acquired tolerance, or had become immune. It is evident that immunity develops very slowly; five weeks of injections gave little protection, and it was only after nearly three months treatment that a high degree of immunity was obtained.

These immune rats were bled, and various mixtures of serum and venom were made. It was found that ½ cc. of the serum added to the venom of 10 spiders completely protected all the rats, which showed no symptoms of poisoning. In other rats, the venom of two spiders was injected, followed after 10 minutes by ½ cc. of serum; no symptoms of poisoning occurred. In other cases 1 cc. of serum caused prompt recovery when given one hour after the venom injection, when symptoms of poisoning were well advanced. When the venom was given subcutaneously, 1 cc. of immune serum, injected intraperitoneally after 3½ hours, was followed by recovery.

There is also some evidence of transmission of antibodies through the placenta, but the immunity is not very marked. It was also found possible to immunize rats against the poison contained in spiders' eggs, and the serum was protective against egg-poison. Experiments showed that spider venom and the poison of the eggs are distinct; neutralization of egg-poison by venom-immunized serum does not occur, nor does the reverse.

A commercial firm was able to immunize sheep against spider venom; the sheep yielded a serum of some potency, ¼ cc. of which

protected rats against the equivalent of two spiders, when given intraperitoneally.

Autopsy of rats killed by spider venom showed no gross pathological lesions, nor any decided histological changes in the organs of the body.

H. J. Walton.

Hargis (A. S.). **Arachnidism.**—*New England Jl. of Med.* 1936. Sept. 10. Vol. 215. No. 11. pp. 489–492. [12 refs.]

A review of the subject of poisoning by the Black Widow spider, *Latrodectus mactans*. The bites are becoming more common, at all events more cases are being recorded. The symptoms may simulate those of " acute abdomen." During the past 15 years 43 patients have been admitted to hospital; admissions have occurred at all seasons, but more in late summer and early autumn. Little is known as yet concerning the poison, but it probably acts on the myoneural terminations. None of the 43 cases studied by the author terminated fatally. [See this *Bulletin*, 1936, Vol. 33, p. 401.] *H. H. S.*

d'Amour (Fred E.). **A Comparative Assay of Black Widow Anti-Sera.** —*Proc. Soc. Experim. Biol. & Med.* 1936. Nov. Vol. 35. No. 2. pp. 262–263.

The author has made assays of human serum from a convalescent from Black Widow spider bite and of immune serum prepared from sheep. His method was to dissect out the venom glands and macerate them in saline, and the average lethal dose for rats was determined, *i.e.*, the amount which caused the death of half the animals tested. Varying amounts of the sera were added to emulsions of the venom, and injected after being in the refrigerator over night. The results are presented in a table and show that the sheep antivenene has a much greater potency; 1 cc. was found to neutralize completely 25 average lethal doses, whereas 1 cc. of the human serum did not neutralize even 2 doses of the venom. [See also this *Bulletin*, 1935, Vol. 32, p. 914, 915; 1936, Vol. 33, p. 401.] *H. H. S.*

Le Gac (P.). Accidents consécutifs à la piqure d'une araignée venimeuse, le *Latrodectus menavodi*. [**Bite by a Venomous Spider,** *Latrodectus menavodi*.]—*Bull. Soc. Path. Exot.* 1936. May 13. Vol. 29. No. 5. pp. 621–622.

A soldier, 23 years of age, was resting on the ground during manoeuvres when he was bitten on the right thigh by a spider. The pain was very severe, of a burning character, and the limb began to feel numb; this numbness soon spread to the left leg also and he could not move his legs. In half an hour the pain extended upwards over the abdomen; violent headache supervened and the arms were benumbed. That evening on arrival in hospital all the limbs seemed paralysed and the patient unconscious; the features were drawn, limbs cold, reflexes lost; the pulse small, uncountable and the body bathed in sweat. Next day the patient still complained of headache, but the paresis had disappeared and he could walk without difficulty, but reflexes were still in abeyance for some hours; pulse 75 per minute.

The following day he left hospital quite recovered. No antivenene was obtainable and the treatment usually followed is intravenous injection of sulphate of magnesium, 25 per cent. solution, and this is found quite successful (the quantity is not stated).

Three species of Latrodectus are found in Madagascar, *L. mactans* or " black widow," *L. hasseltii* or " red-backed spider " and *L. menavodi*. According to Asis the venom has a predilection for the peripheral nerves and their endings, and affects the central nervous system hardly at all. *H. H. S.*

Finlayson (M. H.). **Specific Antivenene in the Treatment of " Knoppie-Spider " Bite.**—*South African Med. Jl.* 1937. Mar. 13. Vol. 11. No. 5. pp. 163–167.

The author has described the preparation of *Latrodectus indistinctus* antivenene and shown that it will also neutralize the venom of *L. concinnus*. In the present article he demonstrates that the venom of *L. indistinctus* is precipitated by *L. concinnus* serum at the same titre as the homologous serum and therefore they probably possess the same antigens. The reverse does not hold good. *L. concinnus* venom is not precipitated so strongly by *L. indistinctus* serum as by the homologous antiserum, *i.e.*, *L. indistinctus* venom possesses an additional antigen. Further experiments showed the activities of *L. indistinctus* antivenene prepared from goats in the treatment of guineapigs inoculated with the venom.

The author goes on to record brief notes of eighteen human patients bitten by the knoppie spider, who received this antivenene, usually in a dose of 5 cc. subcutaneously, but in others 10 cc., or 2·5 cc. plus the same intravenously. Although some were in a state of collapse when the serum was administered, all had practically recovered within 24 hours of receiving it. Though knoppie spider bite is not often fatal, the value of the antivenene has been clearly shown. A large supply is kept for issue at the Biological Control Laboratories, Union Health Department, Cape Town. *H. H. S.*

Finlayson (M. H.). **" Knoppie-Spider " Antivenene.**—*South African Med. Jl.* 1936. Nov. 14. Vol. 10. No. 21. pp. 735–736.

In the Cape Province " knoppie spider-bites " are caused by two species of Latrodectus, *L. indistinctus* and *L. concinnus*, but the venom of either is neutralized by antivenene of the former, which abounds in the sand-veldt areas of the Province.

The author has prepared an antivenene in the following manner :

Heads of the female *L. indistinctus* were extracted at 0°C. with sterile distilled water, and the extracts centrifuged and dried over P_2O_5 at 0°C. three times. The final powder was used as the venom ; it had no haemolytic action on guineapigs' corpuscles.

Goats were inoculated with an initial dose of 5 mgm. of venom and sufficient rabbit antiserum almost to neutralize it. At four-day intervals injections were given of the same amount of venom but decreasing antiserum, and later venom alone in increasing doses. After 3 months the dose reached was 50 mgm. subcutaneously. By 2½ months 0·05 cc. of serum neutralized 1·0 mgm. venom, which was the highest titre

obtained. Mice were used as test animals. 0·2 cc. of a 1 in 5 dilution of antivenene injected 18 hours after 0·3 mgm. of the venom resulted in recovery. 1·0 cc. of the serum will protect mice against 7·5 mgm. of venom or 150 mouse lethal doses.

When, in place of injections of artificially prepared venom, mice were subjected to bites of the spider 0·2 cc. of the antivenene injected subcutaneously 30 minutes after the bite was followed by recovery ; a control mouse and another given 0·1 cc. died within 24 hours. Individual *L. indistinctus* may possess 200 mouse m.l.d. of venom, needing about 1·3 cc. of antivenene. The serum has been put up in ampoules containing 5 cc. which should afford ample protection against accidental bites from this spider. It will be issued free to district surgeons and practitioners in areas where these accidents occur.

H. H. S.

Cheverton (R. L.). **Irritation caused by Contact with the Processionary Caterpillar (Larva of *Thaumetopoea wilkinsoni* Tams) and its Nest.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Feb. 29. Vol. 29. No. 5. pp. 555–557. With 4 figs. on 1 plate.

The moth whose larvae and nests produce the symptoms detailed below is found in Europe, Africa, Madagascar and Cyprus. Contact with the caterpillar or with dust from its nest produces symptoms of severe irritation. The case here recorded is that of a boy who disturbed a nest and by the following day there was marked conjunctivitis, oedema of the face and particularly the eyelids, succeeded in a few days by local superficial gangrene of the lids of the right eye. Three weeks later the gangrenous area had separated leaving a scar, and there was a residual corneal ulcer and conjunctivitis.

The author gives an account of the life history of this moth. Eggs are laid in October ; pupation takes place during March at sea level, a little earlier at higher altitudes up to 4,500 feet. In Cyprus, the nest is from 4–12 inches long, and cone-shaped, white and glistening at first, later brown. When the nest is disturbed or the caterpillar handled, large urticarial wheals appear very rapidly, accompanied by intense irritation. For this reason, entomologists use rubber gloves when handling them. More work is needed to determine the toxic substance, its source and nature. Some think it is the excreta, others the special hairs or spines with poison cells. " These hairs are hollow and contain the poison, each hair having a gland cell opening into the seta, which contains the poisonous secretion ; the fine barbed hairs penetrate the surface causing the poison to spread. The secretion inside the seta retains its urticating properties for a long time . . . ." If the hairs be washed with ether, the extract causes urticaria but the residual hairs no longer have this action. The article has a good illustration of the caterpillar, the nest, the hairs and the patient. *H. H. S.*

Escomel (E.). Envenimation neuro-myopathique par la morsure d'une scolopendre. [**Poisoning by Centipede.**]—*Bull. Soc. Path. Exot.* 1936. Mar. 11. Vol. 29. No. 3. pp. 282–284.

A man was sitting on the trunk of a tree which he had felled and was bitten on the left leg by one of a number of centipedes (Scolopendra)

he had disturbed. In a few moments the place began to itch, then felt tense, and soon after became painful. The leg and foot swelled rapidly and became a dark red, in the middle of the inflamed area the bite was visible. He applied cold compresses and in four days the swelling was diminishing, as were also the other local symptoms, and in a month there was no trace of oedema and merely a little staining of the skin. So much for the local condition. Ten days after the bite he experienced severe headache, of sudden onset, followed by general depression, lassitude and muscular weakness and lay listless in bed. He had till then been a strong and active man. He was slow in cerebration, his memory was bad, there was some incoordination and obstinate insomnia for several days. From time to time he had attacks of shivering; speech was slow and laboured. Four weeks after the bite he consulted the author; he walked supported by a friend's arm; his gaze was vague and somewhat fixed; he got up from a chair with difficulty (not due to pain but to "want of energy"); tendon reflexes present, but diminished. Pulse 60, regular but feeble, muscle-power by dynamometer 75 in right hand, 70 in left; (formerly it had been 100 and 95 respectively). The condition is aptly described as one of neuromyopathy. Treatment was symptomatic. *H. H. S.*

Barros (Evandro da Fonseca). Hyper-sensibilidade ao veneno de marimbondos. [**Susceptibility to Wasp-Sting.**]—*Brasil-Medico.* 1937. Feb. 20. Vol. 51. No. 8. pp. 297–301. English summary.

Polistes canadensis is a domestic wasp of Campos and S. João da Barra, in the State of Rio. It is astonishing that wasp-stings are not more common, for nearly every house has a colony or two attached to the roof or other part where they are not likely to be disturbed. It is, it seems, usually a pacifist, and flies about its business harming no one unless interfered with or its nest is repeatedly attacked. People carry out their usual occupations unmolested and if the wasp settles on them, it does no harm if no attempt is made to drive it away. If, however, they are repeatedly irritated, they become very vicious and will follow the marauder for a considerable distance, especially in nesting time.

Details of seven cases are recorded here. The effects of the sting are: irritant action on the tissues with swelling, oedema, urticaria, and symptoms of constitutional disturbance, such as dyspnoea, sweating, vomiting, anxiety, fall of temperature, and in severe cases more shock, loss of consciousness and even death has been reported. The venom has not yet been studied. *H. H. S.*

Kellaway (C. H.) & Lemessurier (D. H.). **The Venom of the Platypus** (*Ornithorhynchus anatimus*).—*Australian Jl. Experim. Biol. & Med. Sci.* 1935. Dec. 16. Vol. 13. Pt. 4. pp. 205–221. With 12 figs.

On the inside of each hind limb near the ankle the male platypus has a sharp spur which is canalized and conveys the secretion of a crural gland and a wound by this spur results in severe pain, local swelling and symptoms of shock. The author carried out experiments

on cats, rabbits and guineapigs with an old sample of venom and a little obtained from a platypus soon after death. The old sample had but slight coagulant action ; the coagulation time of shed blood in normal animals was prolonged ; this was shown also in citrated plasma *in vitro*. Intravenous injection of the venom is followed at once by marked fall in blood pressure, without intravascular clotting ; it is due to vasodilatation and is peripheral in origin (compare the Australian snake venoms) ; there is no evidence that the carotid sinuses or vagi play any part. The venom has no specific action on the central nervous system, nor any curari-like action peripherally. In brief, platypus venom has a weak coagulant, haemolytic and cytolytic property, but no specific neurotoxic action and the fall of blood pressure is due to peripheral not central action, to vasodilatation.

H. H. S.

REVIEWS AND NOTICES.

STEPHENS (J. W. W.) [M.D., F.R.S., Professor Emeritus of Tropical Medicine, University of Liverpool]. **Blackwater Fever. A Historical Survey and Summary of Observations made over a Century.** With Foreword by Col. Sir S. Rickard CHRISTOPHERS, C.I.E., O.B.E., F.R.S., I.M.S. (ret.).—pp. xvi + 728. With 1 plate. 1937. Liverpool: University Press; London: Hodder & Stoughton Ltd. [15*s.*]

Those who purchase this book under the impression that they are acquiring a work which deals with its subject in the traditional manner will be sadly disillusioned. It is something which in the reviewer's experience is unique. The first impression is so overwhelming that the reader must perforce soon close the volume in order that he may regain his shocked and scattered wits. After a rest—short or long according to the effect of the first impact—he will return to the attack more cautiously, and timidly examine the preface to find out what it is all about. There he will read :—

> I have attempted in the following pages to give an account of blackwater fever since its first recognition as a distinct condition about a century ago.
>
> The extracts given are necessarily brief, and though separated from their context will, I think, suffice to illustrate the development and present state of our knowledge, imperfect though it be, of the various aspects of the blackwater fever problem.
>
> The material has been arranged for the most part in alphabetical order, and the various data in chronological sequence.
>
> These data appear to be of very unequal value, but I have not considered it necessary to express my own opinion of the various records, for their contradictory nature is in itself sufficient to show that they should be very cautiously examined before being accepted as fact.

In this book Stephens has accomplished, as probably he alone could, the gigantic task of gathering together the conflicting mass of statements which has appeared in the literature of this disease from the earliest times. Chapter I, consisting of 6 pages, is devoted to the synonymy, and even the long list of synonyms mentioned here is only a selection from the more complete list given in Appendix I. It is interesting to note that the name blackwater fever was first used by EASMON in 1834. Chapter 2 deals with the geographical distribution, and Chapter 3 with the history of disease going back to the time of Hippocrates (406–370 B.C.). The "Epidemics" contain 42 case-histories and 15 of these cases had black urines and 3 red. These case-histories are summarized in Appendix 2. Disregarding 5 cases in women (4 in child birth and so possibly "puerperal") 13 remained; and in a table Stephens has given an analysis of the symptoms of these 13, which we should expect to find in blackwater fever. The modern history of blackwater fever in Greece begins in 1858.

Chapters 4 to 7 are concerned with aetiology; the first records the general factors which have by various writers been supposed to bear on the matter, the second the reasons for considering malaria as an aetiological factor, and the third and fourth observations on which depends the belief that quinine, cinchona, cinchonine and plasmoquine provoke attacks of blackwater fever.

Chapter 8, consisting of 165 pages, deals with the symptomatology of the disease. Here, as in many parts of the book, the material is

arranged alphabetically, so that the first symptom referred to is "Ascites" and the last is "vomiting."

The remaining four chapters deal with treatment, prognosis and prophylaxis, with changes in the blood, with changes in the urine and faeces, and with the pathology of the disease.

The volume does not, however, close at this point. There follows a series of 25 appendices, which occupy no less than 120 pages. In these appendices the author has collected from the literature the observations bearing on such matters as malaria parasites in blackwater fever, the intervals between quinine and haemoglobinuria, and the day of death. He discusses the history of the discovery of Peruvian bark, its introduction into Europe and the controversies relating to its use in England, France, and elsewhere; the discovery and use of quinine and its toxic effects; and many other matters. The appendices are followed by Addenda and by an enormous list of references.

One of the facts which will most strongly impress anyone who knows the author is the almost complete absence from this book of anything in the way of criticism. The explanation is, however, to be found in the last paragraph of the preface which reads as follows:—

> It will, I think, be evident from this compendium that a complete and accurate epitome of blackwater fever could not be written until the conflicting mass of statements in the literature are harmonized by more precise observation, by the use of modern methods of investigation, and by a much more rigorous use of the critical faculty than has hitherto obtained.

From this it would appear that in Stephens' view criticism in the present state of ignorance could serve no useful purpose. Still it is refreshing to read here and there at the close of a chapter a few lines like the following, which appear at the end of the 57 pages describing the various forms of treatment which have been recommended:—

> The treatments here summarized have been advocated with no more evidence of their efficacy than that the patients (or some of them) survived. In some cases only a single case has been treated! The fact that many cases recover without the use of any special drug or drugs—a fact over and over again ignored—invalidates the claims made.
>
> Of the multitude of treatments used, perhaps saline has the best record, though it should be used cautiously. The evidence as to whether Q. should be given or not is conflicting. It would seem to be unnecessary unless there is evidence to the contrary.
>
> Of modern treatments, transfusion in cases of grave anaemia would appear to be beneficial.

Any reviewer who wrote of this book that it should be on the shelves of every medical man practising in the tropics would quickly be discredited. But this statement is not to be taken as implying that the present reviewer considers the work to be of little value. Far from it; the book is of immense value, but to a more limited clientèle. To the reviewer's mind, Sir Rickard Christophers sums up the matter when he writes in the Foreword:—

> With the present volume in his hand, two thoughts will probably be uppermost in the reader's mind, first, what a mass of facts of a sort have been accumulated, e.g. in the symptomatology so fully set out by the author, and secondly, what a need there is of a really adequate investigation of this disease on modern lines. If Professor Stephens' book has done nothing else, it has given a sort of platform of so far recorded data from which both the medical man and the pure investigator can start square, the first with a means of easily ascertaining what clinical and pathological

observations have been made and what treatments described, and the latter with the jungle of past literature mapped, abstracted and systematised. *W. Yorke.*

Mishnaevsky (M. N.) [Edited by]. [**The Malarial Mosquito and the Measures for combating it.**]—Publ. by the Azov-Black Sea Regional Tropical Institute and the North-Caucasian Regional Institute of Epidemiology and Microbiology. 1937. Rostov-on-Don. 224 pp. With 64 figs. [In Russian.]

This is a practical guide intended for medical officers and others engaged in anti-mosquito measures of prophylaxis of malaria in the South Eastern parts of U.S.S.R. The various aspects of the work are dealt with in four sections. In the first, by I. G. Ioff (" Mosquitoes as malaria vectors and the fight against them "), the morphology and systematics of mosquitoes are briefly disposed of in three keys: one for the determination of the genera of Culicidae, another for the identification of the larvae, and the third for determining the important species of *Anopheles*. The main part of this section is devoted to the biology and ecology of mosquitoes, especially of *A. maculipennis*; to their role in the transmission of malaria, and to the methods used for their destruction and for protection against them. In the second section (" On the organization of antimalarial hydrotechnical works ") the same author describes various types of water collections in which anophelines breed and deals with the antimalarial methods applicable in each case. The third contribution (" Amelioration works in the antimalarial campaign "), by A. A. Dotsenko, is devoted entirely to the hydrotechnical aspect of antimalarial measures: a description is given of methods of surveying water collections, of draining swamps, and of regulating the course of rivers and canals, etc. Finally, V. A. Nabokov (" The aviochemical method of combating the larvae of the malarial mosquito "), describes the methods of distributing larvicidal substances from aeroplanes. *C. A. Hoare.*

Sicé (A.) [Médecin du Corps de Santé Colonial Ancien, Directeur de l'Institut Pasteur de l'A.E.F.]. **La trypanosomiase humaine en Afrique Intertropicale.** Préface de M. le Professeur Mesnil.—pp. xi + 306. With 43 figs. (including 1 map) & 4 plates (2 coloured). [569 refs.] 1937. Paris (VIe): Vigot Frères, Editeurs, 23 rue de l'Ecole-de-Médecine. [50 fr.]

This volume is written by one who has spent many years in the field carefully studying the disease, and who has made many valuable contributions to knowledge of it.

It is divided into 5 chapters, the first of which, apart from a few pages devoted to historical matters, is entirely concerned with the geographical distribution of the disease in different parts of tropical Africa. The second chapter deals with epidemiology; here the author gives an account of the trypanosomes and tsetse flies, and discusses certain factors bearing upon the epidemiology of the disease.

Chapter 3, which is concerned mainly with symptomatology and pathology, is particularly valuable. To anyone familiar with the author's work it is not surprising to find the changes in the cerebro-spinal fluid, and their significance for prognosis and treatment, discussed in great detail. The description of the pathology of the disease is good, and the chapter ends with a consideration of the

various methods of diagnosis. The next chapter is devoted to treatment, and the last to the subject of prophylaxis.

At the end of the volume is a list of 569 references; unfortunately, however, a surprisingly large proportion of the reference numbers given in the text do not relate to the appropriate references. Thus on page 205 we see Zupitza (560), but on turning to reference 560 we see that it relates to a paper by Yorke, Murgatroyd & Hawking; similarly, on page 168 we read Peruzzi (469), whereas the correct reference should be 473. This sort of mistake is very frequent and may prove rather irritating to those who are not very familiar with the literature of the subject.

In the reviewer's opinion, Sicé's book is the best and most comprehensive account of African trypanosomiasis in existence. It is a worthy successor of Laveran et Mesnil's classical work "Trypanosomes et Trypanosomiases," and cannot fail to prove of the highest value to all engaged in an attempt to combat this great scourge of tropical Africa. *W. Yorke.*

LAPAGE (Geoffrey) [M.A., M.D., Institute of Animal Pathology, University of Cambridge]. **Nematodes Parasitic in Animals.**—pp. x + 172. Methuen's Monographs on Biological Subjects. 1937. London: Methuen & Co., Ltd. 36 Essex Street, W.C. [4*s.* 6*d.*]

The object of the publishers in providing the general reader with a brief authoritative account of present knowledge in some specialized branches of the biological sciences has been achieved in an admirable way by Dr. Lapage in this little book on *Nematodes Parasitic in Animals.*

Its scope may be judged from the titles of the four chapters into which the subject matter is divided (1) Structure, life-histories and classification. (2) Physiology. (3) Resistance of host to nematode infestations and (4) The control of nematode infestations.

The method of treatment may be described as "zoology with a medical bias" and is an account of the modern helminthologist's knowledge rather than of the progress of specialized academic zoology. Nevertheless, the author goes into considerable detail over the physiology of these parasites and if one were to offer any criticisms at all it would be to suggest that a too generous proportion of the space had been given to this branch of the subject and a too meagre one to the account of life histories, structure and classification. But the author holds strongly to the view that a better understanding of the physiology of these parasites is the key to the progress of our knowledge at the present time, and there are certainly grounds for that view.

One error has crept in on page 21 where *Dictyocaulus filaria* is represented as requiring the intervention of an invertebrate host for the completion of its life history, the name "Schwartz" is misspelt in several places, and one slight error was noticed in the list of references (seen in a comparison of Nos. 5A and 277) but proof reading on the whole has been well and carefully done.

The text is a clear, concise and uncritical account of the work which has been done on parasitic nematodes, and this, together with the very numerous references to the 404 original publications which are given in the bibliography, renders the book a most readable and useful addition to this series of monographs. *E. L. Taylor.*

WIELENGA (Douwe Klaas). **Onderzoekingen over het scleroma respiratorium en de groep der kapselbacteriën.** [Rhinoscleroma in the Netherlands Indies.] [Thesis for Doctorate of Medicine at Amsterdam University.]—153 pp. With 1 map, 5 graphs & 12 figs. on 3 plates. [113 refs.] English summary pp. 145–148. 1937. Amsterdam : N.V. Noord-Hollandsche Uitgeversmaatschappij.

This work is an excellent review and study of a condition which is common in the Netherlands Indies and seen, though less commonly, in the United States and in South America. The subject is dealt with in six chapters. The first contains a review of recent literature of a critical character and a consideration of the chief diagnostic features. Clinical signs alone are not adequate, the finding of *Klebsiella scleromatis* should be regarded as essential. Evidence of contagiousness is accumulating. The second chapter recounts its prevalence in the Netherlands Indies, 70 cases being known in the Batak area, 42 in Bali, 15–20 in the Minahasse and rather fewer in Java and other parts. Foci seem to be scattered along lines of travel. The author breaks new ground in suggesting that gangosa may be a special manifestation of the disease. Next follow chapters on the bacteriology and serology of the condition. To obtain good growth of the Klebsiella material should be taken from the deeper layers of the tissue and not from the nasal mucus. Identification and differentiation from other organisms are made by a study of the capsule antigens, for details of which the original must be consulted. The fifth chapter gives an account of an investigation of the nasal flora and shows that the organism in question is absent from normal subjects and that the idea that it is ubiquitous and a chance concomitant is not tenable. Finally, the author's attempts to reproduce the condition in animals by inoculation are described. Though scleroma could not be produced, in the liver and spleen of the experimental animals, monkeys, rats and mice, cells indistinguishable from Mikulicz cells were seen and these are a characteristic feature of human scleroma tissue. The book is furnished with a fairly full bibliography of more than a hundred references. There are two photographs of patients showing well the condition and several well-reproduced photomicrographs of the organism, cultures and pathological histology. *H. H. S.*

SOEHARTO (Raden). **Over zweren in maag en duodenum bij Inheemschen en Chineezen in Nederlandsch-Indië.** [Gastric and Duodenal Ulcers in Chinese and Malays.] [Thesis for Doctorate of Medicine, Medical High School, Batavia.]—93 pp. [38 refs.] 1937. Batavia-C. : G. Kolff & Co.

[Geographical, racial and sex differences in the incidence of disease may serve to throw light on causation and are well worth investigating. The subject of the incidence of gastric and duodenal ulcers in Malays and Chinese has received considerable attention from workers in the Netherlands Indies and reference may be made to KOUWENAAR (this *Bulletin*, 1931, Vol. 28, p. 42) and BRUMMELKAMP (this *Bulletin*, 1934, Vol. 31, p. 349).] The author reaches the same conclusions as these authors regarding the significantly greater incidence of gastric ulcer in Chinese men than in Malays, as previous workers have done. On the other hand duodenal ulcer is not so common in Chinese men as gastric ulcer ; the reverse is the case among the Malays. In statistics such

as these, the age distribution of the several populations has to be taken into account and this is done by the author when he restricts his principal figures of comparison to persons older than 20 years. For Chinese males, Chinese females, Malay males and Malay females the percentages of incidence, as determined in the post-mortem room, were respectively: gastric ulcer, 3·6, 0·6, 0·3 and 0·4 per cent.; duodenal ulcer, 2, 0·6, 0·4 and 0·5 per cent. Probable errors accompany these percentages. No explanation is forthcoming of the reasons for the differences between Chinese men and Malay men or for those between Chinese men and women. *W. F. Harvey.*

i. Mitchell (John P.) [O.B.E., M.D., Med. Supt., Mulago Hospital & Principal of the Uganda Medical School]. **Anatomy and Physiology and Causes of Disease.**—pp. xvi + 215. With 87 figs. Baillière's Medical Manuals for Africans. Vol. 1. 1937. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, Covent Garden, W.C.2. [2*s.* 6*d.*]

ii. Bagot (Ruth A.) [M.B.E., Lady Superintendent of Nurses, Uganda]. **Nursing.**—pp. xii + 183. With 136 figs. Baillière's Medical Manuals for Africans. Vol. II. 1937. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, Covent Garden, W.C.2. [2*s.* 6*d.*]

These small volumes comprise two of a series of handbooks written for the instruction of African nurses, dispensers and health orderlies, the first by the principal of the Uganda Medical School, the second by the lady superintendent of nurses, Uganda.

i. Dr. Mitchell in the first part of his book has succeeded in giving, in 155 pages, an account of the elements of anatomy and physiology which is simple and clear. In the second part of only 50 pages he deals with the causes of disease including the whole of parasitology. This very abridged account of a subject, which is of such overwhelming importance in tropical Africa, seems hardly adequate. It may be all that the author deems it necessary to teach his native students, but it might well be worthy of a separate volume. The author states " an endeavour has been made, while avoiding a child-like style, to simplify the text by excluding idiomatic expressions " and in this he is to be congratulated.

It is not obvious why in a book of this kind references are made to Harvey, Pasteur and Lister to the exclusion of all others, nor does it appear relevant to drag in the story of David and Goliath when dealing with the thymus and pineal glands.

ii. Miss Bagot has had an easier task, her contribution might well have been written for use by nurses in this country. The principles underlying the practice of nursing and the methods to be adopted in treating the patient are well displayed. The book will be found a most useful one, and the introduction upon nursing ethics and hospital etiquette are worthy of red lettering.

In anticipation of a second edition in the near future there are a few points which might be added with advantage.

It is advised that iron beds be treated with pesterine to prevent bug infestation. It might be worth while saying what pesterine is and give some alternative method. Lice and delousing are not mentioned. Nail brushes " are to be boiled once a day " but mention is not made of how they should be stored. The washing of mugs, feeders, sputum

mugs, bed pans, urinals, etc. is refered to, but the place where they are to be washed receives no notice and the disinfection of the latter articles is only advised apparently in enteric fever and dysentery. Soiled dressings are to be thrown into a dust bin, but the type of bin and cover and the disposal of its contents are not dealt with. The expression " linen soiled with faeces must be mopped out " is not clear. One is sorry to see that though reference is made to the necessity of treating the folds of the buttock, the groins and the under surfaces of the breasts by washing, etc., nothing is said, as usual, about the genitals. This is a black spot in nursing all the world over. There are three points upon which many will disagree with the author : the routine use of castor oil in preparation for operation, the use of soap in a simple enema, and the giving of sugar cane (sic) for 3 days before operation. Omissions are few, but under causes of offensive sputum no mention is made of bronchiectasis. More might have been said in regard to diet ; only two diets are mentioned, that for typhoid and that for pneumonia. In regard to the former it appears dangerous to the reviewer to include sugar cane ! There is no reference to mosquito nets. *H. S. Stannus.*

CURRENT TITLES FROM BIOLOGICAL JOURNALS. A REGISTER OF SELECTED TABLES OF CONTENTS. 1937. May. Vol. 1. No. 1. 76 pp. [Review appears also in *Bulletin of Hygiene.*]

The new periodical " Current Titles from Biological Journals " promises to render a useful service to biologists and other research workers by providing them, at small cost and promptly, with photo-printed copies of the tables of contents of current bio-medical journals, so that they may select for themselves the articles likely to have a bearing on their work from the hundreds of journals being published in their own and related fields. The first number of " Current Titles " issued in May 1937, gives 147 tables of contents from selected journals published in the weeks immediately preceding its appearance. These journals include 40 dealing with general biology and medicine, 15 with anatomy, 22 with bacteriology, immunology and public health, 13 with parasitology and tropical medicine, and 30 with physiology, biochemistry and pharmacology. Those wishing to receive " Current Titles " for the remaining months of 1937 can do so on sending a remittance of $1.50 to the Editor (L. R. KUHN) 5603, Drexel Avenue, Chicago, Illinois, U.S.A. *R. L. S.*

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